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AT 18:36:41 ON 05 JUN 2001
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L9            7 L3 AND AMINO ACID SUBSTITUTION

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=> s allergen

L10       91377 ALLERGEN

=> s l10 and modified
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L11 2043 L10 AND MODIFIED

=> s l11 and amino acid substitution

L12 7 L11 AND AMINO ACID SUBSTITUTION

=> dup remove l12

PROCESSING COMPLETED FOR L12
L13 4 DUP REMOVE L12 (3 DUPLICATES REMOVED)

=> d l13 1-4 cbib abs

L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2001 ACS
1998:682138 Document No. 129:301697 Mutants of grass **allergens** not recognized by IgE of allergic patients and their use in specific immunotherapy. Kahlert, Helga; Stuwe, Hans-Thomas; Fiebig, Helmut; Cromwell, Oliver; Becker, Wolf-Meinhard; Bufe, Albrecht; Schramm, Gabriele; Jager, Lothar; Muller, Wolf-Dieter (Merck Patent G.m.b.H., Germany). PCT Int. Appl. WO 9843657 A2 19981008, 58 pp. DESIGNATED STATES: W: HU, JP, PL, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (German). CODEN: PIXXD2. APPLICATION: WO 1998-EP1507 19980316. PRIORITY: DE 1997-19713001 19970327.
AB Mutants of **allergens** of a grass (Phleum pratense) that stimulate the lymphocyte proliferation and cytokine synthesis in sufferers of pollen allergies, but have significantly lower binding to serum IgE antibodies of patients are described. The **allergens** can be manufd. by expression of the cloned gene for use in immunotherapy of grass allergies. Specifically, the T-cell epitopes of the **allergens** are **modified** and the modification may arise from a spontaneous mutation or by site-specific mutagenesis. T cell epitopes of the Phl p 5 **allergen** were identified and **allergen** derivs. lacking the most significant ones were prepd. by site-directed mutagenesis involving **amino acid substitutions** and deletions. The derivs. showed very little **allergen** activity as judged by their inability to inhibit IgE binding to wild-type **allergen**.

L13 ANSWER 2 OF 4 MEDLINE DUPLICATE 1
1998224476 Document Number: 98224476. PubMed ID: 9564806. Antagonistic peptides specifically inhibit proliferation, cytokine production, CD40L expression, and help for IgE synthesis by Der p 1-specific human T-cell clones. Fasler S; Aversa G; de Vries J E; Yssel H. (Human Immunology Department, DNAX Research Institute for Molecular and Cellular Biology, Palo Alto, Calif, USA.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1998 Apr) 101 (4 Pt 1) 521-30. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB BACKGROUND: Allergic disorders are characterized by IgE antibody responses to a multitude of **allergens** as a result of the ability of these antibodies to specifically bind to high-affinity IgE receptors on mast cells and basophils. This interaction results in receptor activation and

release of soluble mediators such as histamine and leukotrienes, which cause allergic reactions in various target organs. Because the synthesis of IgE is tightly regulated by cytokines and CD40 ligand (L) interactions, CD4+ helper T cells are obvious targets, with the aim to modulate **allergen**-induced IgE responses. OBJECTIVES: Because of the central role of **allergen**-specific T-helper type 2 (TH2) cells in the pathway leading to IgE synthesis in vitro and in vivo, we have evaluated the possibility of inhibiting **allergen**-induced activation of these cells by using **allergen**-derived peptides that have been **modified** by single **amino acid substitutions**. METHODS: Three cloned human TH2-like CD4+ T-cell lines, specific for Der p 1, the major **allergen** in house dust, were used in this study. Upon activation with Der p 1 or specific Der p 1-derived wild-type peptides, these T-cell clones produce high levels of IL-4 and IL-5 and low levels of interferon-gamma and IL-2, respectively, and furthermore give help to B cells for the production of IgE in vitro. **Modified** synthetic peptides were generated by the introduction of single **amino acid substitutions** into two different T-cell activation-inducing epitopes on Der p 1. The effects of these **modified** peptides were studied in Der p 1-induced proliferation, cytokine production, and in vitro IgE production assays. RESULTS: Several substituted Der p 1-derived peptides failed to induce T-cell proliferation, in contrast to the native peptides. In addition, some of these peptides acted as antagonists by strongly inhibiting wild-type peptide-induced proliferation as well as the production of interferon-gamma, IL-2, IL-4, and IL-5, although the production of the latter two cytokines was less affected than that of interferon-gamma, even at a 100-fold molar excess of the antagonistic peptides. In addition, the presence of an excess of each of the antagonistic peptides during the activation of Der p I-specific T-cell clones prevented induction of CD40L expression, resulting in a failure of these cells to give help to B cells for the production of IgE in vitro, even in the presence of exogenous IL-4. CONCLUSIONS: Substitution of certain amino acid residues in immunogenic Der p 1-derived peptides results in the generation of peptides that fail to induce proliferation of Der p 1-specific T-cell clones. In addition, these **modified** peptides have strong antagonistic activities on Der p 1-induced proliferation, cytokine production, and CD40L expression by **allergen**-specific T-cell clones as well as on T cell-mediated IgE production by B cells. These findings suggest that **modified** peptides interfere with **allergen**-induced activation of T cells, including the production of cytokines and the expression of surface molecules important for successful T cell-B cell interactions, and may therefore have therapeutic potential by inhibiting the expansion and function of **allergen**-specific TH2 cells.

L13 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
1998:257635 Document No.: PREV199800257635. Antagonistic peptides specifically inhibit proliferation, cytokine production, CD40L expression, and help for IgE synthesis by Der p 1-specific human T-cell clones. Fasler, Stephan; Aversa, Gregoria; De Vries, Jan E.; Yssel, Hans (1). (1) INSERM U454, Hopital Arnaud de Villeneuve, 371 Ave. Doyen Gaston Giraud, 34295 Montpellier Cedex France. Journal of Allergy and Clinical Immunology, (April, 1998) Vol. 10, No. 4 PART 1, pp. 521-530. ISSN: 0091-6749.

Language: English.
AB Background: Allergic disorders are characterized by IgE antibody responses to a multitude of **allergens** as a result of the ability of these antibodies to specifically bind to high-affinity IgE receptors on mast cells and basophils. This interaction results in receptor activation and release of soluble mediators such as histamine and leukotrienes, which cause allergic reactions in various target organs. Because the synthesis of IgE is tightly regulated by cytokines and CD40 ligand (L) interactions, CD4+ helper T cells are obvious targets, with the aim to modulate **allergen**-induced IgE responses. Objectives: Because of the central role of **allergen**-specific T-helper type 2 (TH2) cells in the pathway leading to IgE synthesis in vitro and in vivo, we have evaluated the possibility of inhibiting **allergen**-induced activation of these cells by using **allergen**-derived peptides that have been **modified** by single **amino acid substitutions**. Methods: Three cloned human TH2-like CD4+ T-cell lines, specific for Der p 1, the major **allergen** in house dust, were used in this study. Upon activation with Der p 1 or specific Der p 1-dervived wild-type peptides, these T-cell clones produce high levels of IL-4 and IL-5 and low levels of interferon-gamma and IL-2, respectively, and furthermore give help to B cells for the production of IgE in vitro. **Modified** synthetic peptides were generated by the introduction of single **amino acid substitutions** into two different T-cell activation-inducing epitopes on Der p 1. The effects of these **modified** peptides were studied in Der p 1-induced proliferation, cytokine production, and in vitro IgE production assays. Results: Several substituted Der p 1-derived peptides failed to induce T-cell proliferation, in contrast to the native peptides. In addition, some of these peptides acted as antagonists by strongly inhibiting wild-type peptide-induced proliferation as well as the production of interferon-gamma, IL-2, IL-4, and IL-5, although the production of the latter two cytokines was less affected than that of interferon-gamma, even at a 100-fold molar excess of the antagonistic peptides. In addition, the presence of an excess of each of the antagonistic peptides during the activation of Der p I-specific T-cell clones prevented induction of CD40L expression, resulting in a failure of these cells to give help to B cells for the production of IgE in vitro, even in the presence of exogenous IL-4. Conclusions: Substitution of certain amino acid residues in immunogenic Der p 1-derived peptides results in the generation of peptides that fail to induce proliferation of Der p 1-specific T-cell clones. In addition, these **modified** peptides have strong antagonistic activities on Der p 1-induced proliferation, cytokine production, and CD40L expression by **allergen**-specific T-cell clones as well as on T cell-mediated IgE production by B cells. These findings suggest that **modified** peptides interfere with **allergen**-induced activation of T cells, including the production of cytokines and the expression of surface molecules important for successful T cell-B cell interactions, and may therefore have therapeutic potential by inhibiting the expansion and function of **allergen**-specific TH2 cells.

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2001 ACS
1993:579195 Document No. 119:179195 T cell epitopes of the major **allergens** from Dermatophagoides (house dust mite). Garman, Richard D.; Greenstein, Julia L.; Kuo, Mei Chang; Rogers, Bruce L.

(Immulogic Pharmaceutical Corp., USA). PCT Int. Appl. WO 9308279 A1 19930429, 176 pp. DESIGNATED STATES: W: AU, CA, FI, HU, JP, KR, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US8637 19921015. PRIORITY: US 1991-777859 19911016; US 1992-881396 19920508.

AB The 4 **allergens** were immunoaffinity-purified from spent mite culture media. Recombinant **allergens** were also prepd. by cloning and expressing the cDNA in BL21 cells; amino acid sequence polymorphisms were discovered. T cell epitopic studies and cross reactivity studies are shown. There was no detectable IgE reactivity to any of 56 T cell epitopic peptides screened.

=> d his

(FILE 'HOME' ENTERED AT 18:31:19 ON 05 JUN 2001)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 18:31:32 ON 05 JUN 2001

L1 91377 S ALLERGEN
L2 2043 S L1 AND MODIFIED
L3 804 S L2 AND IGE
L4 114 S L3 AND IGE BINDING
L5 3 S L4 AND IGG BINDING
L6 3 DUP REMOVE L5 (0 DUPLICATES REMOVED)
L7 1 S L4 AND AMINO ACID SUBSTITUTION
L8 105 S L3 AND AMINO ACID
L9 7 S L3 AND AMINO ACID SUBSTITUTION

FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 18:36:53 ON 05 JUN 2001

L10 91377 S ALLERGEN
L11 2043 S L10 AND MODIFIED
L12 7 S L11 AND AMINO ACID SUBSTITUTION
L13 4 DUP REMOVE L12 (3 DUPLICATES REMOVED)

=> s l11 and amino acid deletion

L14 0 L11 AND AMINO ACID DELETION

=> s l11 and amino acid addition

L15 0 L11 AND AMINO ACID ADDITION

=> s l11 and IgE binding

L16 114 L11 AND IGE BINDING

=> s l16 and decrease

L17 4 L16 AND DECREASE

=> dup remove l17

PROCESSING COMPLETED FOR L17
L18 2 DUP REMOVE L17 (2 DUPLICATES REMOVED)

=> d l18 1-2 cbib abs

L18 ANSWER 1 OF 2 MEDLINE DUPLICATE 1
97414840 Document Number: 97414840. PubMed ID: 9269506. Preseasonal specific immunotherapy with **modified** Phleum pratense allergenic extracts: tolerability and effects. Ricca V; Ciprandi G; Pesce G; Riccio A; Varese P; Pecora S; Canonica G W. (Servizio di Allergologia, Ospedale Koelliker de Missionari di Maria S.S. Consolata, Torino, Italia.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1997 Jul-Aug) 25 (4) 167-75. Journal code: 3AH; 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB The preparation of chemically **modified allergens**, with a reduced **IgE binding** capacity (responsible for side effects with traditional immunotherapy) but with the same or greater immunogenic activity, is one of the paths followed to obtain better results with specific immunotherapy (IT). The aim of the study was to evaluate the tolerability and effects of an extract Phleum pratense, **modified** with glutaraldehyde and absorbed on aluminium hydroxide, in controlling the seasonal symptomatology induced by grass pollen in a group of 10 monosensitized patients, compared to a group of 10 similar patients not treated with specific IT but with drugs alone. The monitoring parameters were: 1) Clinical: a) symptomatology after specific conjunctival provocation test (pre and post seasonal) and during the natural exposure to the **allergen** b) drug consumption. 2) Immunological (peripheral blood eosinophils, total and specific IgE, total specific IgG). 3) Cytological, before, during and after the pollen season.
CONCLUSIONS: In subjects treated with specific IT a) both the overall symptomatology and the drug consumption resulted significantly reduced compared to the controls ($p = 0.045$); b) the phlogistic infiltrate showed a tendency to **decrease** during the pollen season; c) the peripheral blood eosinophils, total and specific IgE and IgG did not show any significant variation compared to the controls; d) no systemic reactions occurred and there were only two slight local reactions.

L18 ANSWER 2 OF 2 MEDLINE DUPLICATE 2
97163754 Document Number: 97163754. PubMed ID: 9010561. Preseasonal specific immunotherapy with **modified** phleum pratense allergenic extracts: tolerability and effects. Vittorio R; Giorgio C; Giampaola G; Annamaria R; Paola V; Silvia P; Walter C G. (Servizio di allergologia, ospedale koelliker dei missionari di Maria S.S. Consolata, Torino, Italia.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1996 Nov-Dec) 24 (6) 255-62. Journal code: 3AH; 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB The preparation of chemically **modified allergens**, with a reduced **IgE binding** capacity (responsible for side effects with traditional immunotherapy) but with the same or greater immunogenic activity, is one of the paths followed to obtain better results with specific immunotherapy (IT). The aim of the study was to evaluate the tolerability and effects of extracts of Phleum pratense, **modified** with glutaraldehyde and absorbed on aluminium hydroxide, in controlling the seasonal symptomatology induced by grass pollen in a group of 10 monosensitized patients, compared to a group of 10 similar

patients not treated with specific IT but with drugs alone. The monitoring parameters were: 1) Clinical: a) symptomatology after specific conjuctival provocation test (pre and post seasonal) and during the natural exposure to the **allergen** b) drug consumption. 2) Immunological (peripheral blood eosinophils, total and specific IgE, total specific IgG). 3) Cytological, before, during and after the pollen season. Conclusions: in subjects treated with specific IT a) both the overall symptomatology and the drug consumption resulted significantly reduced compared to the controls (p = 0.045); b) the phlogistic infiltrate showed a tendency to **decrease** during the pollen season; c) the peripheral blood eosinophils, total and specific IgE and IgG did not show any significant variation compared to the controls; d) no systemic reactions occurred and there were only two slight local reactions.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 18:31:32 ON 05 JUN 2001

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L1         91377 S ALLERGEN
L2          2043 S L1 AND MODIFIED
L3           804 S L2 AND IGE
L4           114 S L3 AND IGE BINDING
L5             3 S L4 AND IGG BINDING
L6             3 DUP REMOVE L5 (0 DUPLICATES REMOVED)
L7             1 S L4 AND AMINO ACID SUBSTITUTION
L8           105 S L3 AND AMINO ACID
L9             7 S L3 AND AMINO ACID SUBSTITUTION
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FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 18:36:53 ON 05 JUN 2001

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L10        91377 S ALLERGEN
L11         2043 S L10 AND MODIFIED
L12            7 S L11 AND AMINO ACID SUBSTITUTION
L13            4 DUP REMOVE L12 (3 DUPLICATES REMOVED)
L14            0 S L11 AND AMINO ACID DELETION
L15            0 S L11 AND AMINO ACID ADDITION
L16          114 S L11 AND IGE BINDING
L17            4 S L16 AND DECREASE
L18            2 DUP REMOVE L17 (2 DUPLICATES REMOVED)
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=> dup remove l16

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PROCESSING COMPLETED FOR L16
L19           49 DUP REMOVE L16 (65 DUPLICATES REMOVED)
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=> d l19 1-49 cbib abs

L19 ANSWER 1 OF 49 CAPLUS COPYRIGHT 2001 ACS
2001:370416 Characterization and identification of **allergen** epitopes: recombinant peptide libraries and synthetic, overlapping peptides. Reese, G.; Ayuso, R.; Leong-Kee, S. M.; Plante, M. J.; Lehrer,

S. B. (Department of Medicine, Clinical Immunology and Allergy Section, Tulane University Medical Center, New Orleans, LA, 70112, USA). J. Chromatogr., B: Biomed. Sci. Appl., 756(1-2), 157-163 (English) 2001. CODEN: JCBBEP. ISSN: 0378-4347. Publisher: Elsevier Science B.V..

AB For the understanding of the relationship between protein structure and allergenicity, it is important to identify allergenic epitopes. Two methods to characterize primarily linear epitopes are compared using the major **allergen** from brown shrimp (Penaeus aztecus), Pen a 1, as an example. A recombinant peptide library was constructed and synthetic, overlapping peptides, spanning the entire Pen a 1 mol., were synthesized and tested for specific IgE reactivity. Both methods identified **IgE-binding** of Pen a 1, however, the SPOTs procedure resulted in the identification of more epitopes of the major shrimp **allergen** Pen a 1 than the usage of the recombinant peptide library. For detection of specific IgE antibodies, the usage of 125I-labeled detection antibody seems to be superior over enzyme-labeled anti IgE antibodies. The regeneration of SPOTs membranes is possible, but it is prudent to test regenerated membranes for residual activity. If a given food **allergen** contains significant linear epitopes, which seems to be true for stable major **allergens** such as those of peanut and shrimp the SPOTs system may be more advantageous than the use of recombinant peptides libraries. However, if **allergens** are studied that contain more conformational epitopes, recombinant peptide libraries may help to identify the relevant epitopes. It has to be emphasized that no system for epitope identification will detect all epitopes and that the relevance of identified epitopes has to be confirmed with other methods such as inhibition studies, crystallog. anal. or the immunol. evaluation of **modified** whole **allergens**.

L19 ANSWER 2 OF 49 MEDLINE DUPLICATE 1

2001262411 Document Number: 21203243. PubMed ID: 11306930. Engineering, characterization and in vitro efficacy of the major peanut **allergens** for use in immunotherapy. Bannon G A; Cockrell G; Connaughton C; West C M; Helm R; Stanley J S; King N; Rabjohn P; Sampson H A; Burks A W. (Department of Biochemistry and Molecular Biology, Arkansas Children's Hospital Research Institute, Little Rock 72205, USA.. bannongarya@exchnage.uams.edu) . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 70-2. Journal code: BJ7; 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Numerous strategies have been proposed for the treatment of peanut allergies, but despite the steady advancement in our understanding of atopic immune responses and the increasing number of deaths each year from peanut anaphylaxis, there is still no safe, effective, specific therapy for the peanut-sensitive individual. Immunotherapy would be safer and more effective if the **allergens** could be altered to reduce their ability to initiate an allergic reaction without altering their ability to desensitize the allergic patient. METHODS: The cDNA clones for three major peanut **allergens**, Ara h 1, Ara h 2, and Ara h 3, have been cloned and characterized. The **IgE-binding** epitopes of each of these **allergens** have been determined and amino acids critical to each epitope identified. Site-directed mutagenesis of the **allergen** cDNA clones, followed by recombinant production of the **modified allergen**, provided the reagents necessary to test our hypothesis that hypoallergenic proteins are

effective immunotherapeutic reagents for treating peanut-sensitive patients. **Modified** peanut **allergens** were subjected to immunoblot analysis using peanut-positive patient sera IgE, T cell proliferation assays, and tested in a murine model of peanut anaphylaxis. RESULTS: In general, the **modified allergens** were poor competitors for binding of peanut-specific IgE when compared to their wild-type counterpart. The **modified allergens** demonstrated a greatly reduced **IgE-binding** capacity when individual patient serum IgE was compared to the binding capacity of the wild-type **allergens**. In addition, while there was considerable variability between patients, the **modified allergens** retained the ability to stimulate T cell proliferation. CONCLUSIONS: These **modified allergen** genes and proteins should provide a safe immunotherapeutic agent for the treatment of peanut allergy. Copyright 2001 S. Karger AG, Basel

L19 ANSWER 3 OF 49 CAPLUS COPYRIGHT 2001 ACS

2000:666624 Document No. 133:251267 Immunostimulatory nucleic acids and antigens. Sosin, Howard B.; Caplan, Michael J. (Panacea Pharmaceuticals, Llc, USA). PCT Int. Appl. WO 2000054803 A2 20000921, 103 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US7213 20000316. PRIORITY: US 1999-PV124595 19990316; US 1999-PV125071 19990317.

AB The present invention provides methods and compns. for modulating an individual's immune response to antigens. It is an aspect of the present invention that allergic responses to antigens, which in some cases lead to asthma and even anaphylaxis, can be treated or prevented by administering compns. having immunostimulatory oligonucleotides having unmethylated CpG sequences. It is another aspect of the present invention that allergies to antigens, esp. one that result in asthma and anaphylaxis, can be treated or prevented by administering compns. contg. immunostimulatory oligonucleotides having unmethylated CpG dinucleotide sequences and further comprising antigen(s), fragments of the antigen, mixts. of fragments of the antigen, antigens **modified** to reduce Th2-type immune responses, and fragments of the antigen **modified** to reduce Th2-type immune responses. Cellular systems for studying immunostimulation by CpG contg. nucleic acids include in vivo, in vitro or ex vivo systems.

L19 ANSWER 4 OF 49 CAPLUS COPYRIGHT 2001 ACS

2000:628260 Document No. 133:221613 Site-specific mutated **allergens** for decreased clinical reaction to allergy. Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A.; Sosin, Howard B.; King, Nina E.; Maleki, Soheila J.; Connaughton, Cathie; Kopper, Randall A.; Rabjohn, Patrick A.; Shin, David S.; Compadre, Cesar M. (The Board of Trustees of the University of Arkansas, USA; Mount Sinai School of Medicine of New York University). PCT Int. Appl. WO 2000052154 A2 20000908, 38 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,

IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US5487 20000302. PRIORITY: US 1999-PV122566 19990302; US 1999-PV122960 19990303; US 1999-267719 19990311; US 2000-494096 20000128.

AB It has been detd. that **allergens**, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be **modified** to be less allergenic by modifying the **IgE-binding** sites. The **IgE binding** sites can be converted to non-**IgE binding** sites by masking the site with a compd. that prevents **IgE binding** or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the **IgE-binding** epitope, to eliminate **IgE binding**. The method allows the protein to be altered as minimally as possible, other than within the **IgE-binding** sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of **IgE-binding** sites. The crit. amino acids within each of the **IgE-binding** epitopes of the peanut protein that are important to Ig binding were detd. Substitution of even a single amino acid within each of the epitopes led to loss of **IgE binding**. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to **IgE binding** .

L19 ANSWER 5 OF 49 MEDLINE DUPLICATE 2

2000429040 Document Number: 20384768. PubMed ID: 10925258. T cell reactivity with allergoids: influence of the type of APC. Kahlert H; Grage-Griebenow E; Stuwe H T; Cromwell O; Fiebig H. (Allergopharma Joachim Ganzer KG, Reinbek, Germany.. allergopharmakg@csi.com) . JOURNAL OF IMMUNOLOGY, (2000 Aug 15) 165 (4) 1807-15. Journal code: IFB; 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The use of allergoids for **allergen**-specific immunotherapy has been established for many years. The characteristic features of these chemically **modified allergens** are their strongly reduced **IgE binding** activity compared with the native form and the retained immunogenicity. T cell reactivity of chemically **modified allergens** is documented in animals, but in humans indirect evidence of reactivity has been concluded from the induction of **allergen**-specific IgG during immunotherapy. Direct evidence of T cell reactivity was obtained recently using isolated human T cells. To obtain further insight into the mechanism of action of allergoids, we compared the Ag-presenting capacity of different APC types, including DC and macrophages, generated from CD14+ precursor cells from the blood of grass pollen allergic subjects, autologous PBMC, and B cells. These APC were used in experiments together with Phl p 5-specific T cell clones under stimulation with grass pollen **allergen** extract, rPhl p 5b, and the respective allergoids. Using DC and macrophages,

allergoids exhibited a pronounced and reproducible T cell-stimulating capacity. Responses were superior to those with PBMC, and isolated B cells failed to present allergoids. Considerable IL-12 production was observed only when using the DC for Ag presentation of both **allergens** and allergoids. The amount of IL-10 in supernatants was dependent on the phenotype of the respective T cell clone. High IL-10 production was associated with suppressed IL-12 production from the DC in most cases. In conclusion, the reactivity of Th cells with allergoids is dependent on the type of the APC.

L19 ANSWER 6 OF 49 MEDLINE DUPLICATE 3
2000385116 Document Number: 20307538. PubMed ID: 10848918. Cloning of the minor **allergen** Api g 4 profilin from celery (Apium graveolens) and its cross-reactivity with birch pollen profilin Bet v 2. Scheurer S; Wangorsch A; Haustein D; Vieths S. (Paul Ehrlich Institute, Department of Allergology, Paul Ehrlich Street 51-59, D-63225 Langen, Germany.) CLINICAL AND EXPERIMENTAL ALLERGY, (2000 Jul) 30 (7) 962-71. Journal code: CEB; 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: Profilin is a panallergen that is recognized by IgE from about 20% of birch pollen- and plant food-allergic patients. A subgroup of celery-allergic patients shows IgE-reactivity with this minor **allergen**. To investigate the **IgE-binding** potential and cross-reactivity of celery profilin at the molecular level, this study was aimed at the cloning and immunological characterization of this **allergen**. OBJECTIVES: Cloning, expression and purification of profilin from celery tuber to characterize its immunological properties and its cross-reactivity with birch pollen profilin. METHODS: Cloning of celery profilin was performed by polymerase chain reaction using degenerated primers and a 5'RACE method for the identification of the unknown 5'-end of the cDNA. Expression was carried out in Escherichia coli BL21 (DE3) using a **modified** vector pET-30a. The recombinant profilin was purified by affinity chromatography on poly L-proline coupled to sepharose. Immunological characterization was performed by immunoblotting, EAST and IgE-inhibition experiments. RESULTS: The coding region of the cDNA of celery profilin was identified as a 399-bp open reading frame, coding for a protein of 133 amino acids with a calculated molecular weight of 14.3 kDa. The deduced amino acid sequence of the corresponding protein showed high identity with other plant profilins (71-82%) recently described as **allergens**. Celery profilin was isolated as highly pure nonfusion protein. The IgE-reactivity of celery profilin was similar to that of natural protein. Seven of 17 celery-allergic patients tested presented specific IgE-antibodies to the recombinant protein tested by immunoblotting. Inhibition experiments showed high cross-reactivity of IgE with both profilins from celery and birch pollen. Moreover, the biological activity of recombinant celery profilin was demonstrated by a histamine release assay. CONCLUSIONS: Celery profilin is an important allergenic compound in celery and shows high homology to birch pollen profilin, Bet v 2. According to the revised IUIS **allergen** nomenclature, we suggest naming the celery profilin Api g 4. In addition to the cross-reacting major

allergens Api g 1 and Bet v 1, birch pollinosis and associated allergies to celery can therefore additionally be explained by the cross-reactivity between homologous profilins. Moreover, recombinant Api g 4 may be used for target-specific diagnosis and structural analyses.

L19 ANSWER 7 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:404901 The Genuine Article (R) Number: 317QM. Mechanisms of **allergen**-specific immunotherapy. Akdis C A; Blaser K (Reprint). SWISS INST ALLERGY & ASTHMA RES, OBERE STR 22, CH-7270 DAVOS, SWITZERLAND (Reprint); SWISS INST ALLERGY & ASTHMA RES, CH-7270 DAVOS, SWITZERLAND. ALLERGY (JUN 2000) Vol. 55, No. 6, pp. 522-530. Publisher: MUNKSGAARD INT PUBL LTD. 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK. ISSN: 0105-4538. Pub. country: SWITZERLAND. Language: English.

L19 ANSWER 8 OF 49 MEDLINE DUPLICATE 4
2000290936 Document Number: 20290936. PubMed ID: 10828721. Modulation of **allergen**-specific immune responses to the major shrimp **allergen**, tropomyosin, by specific targeting to scavenger receptors on macrophages. Rajagopal D; Ganesh K A; Subba Rao P V. (Department of Biochemistry, Indian Institute of Science, Bangalore, India.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2000 Apr) 121 (4) 308-16. Journal code: BJ7; 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.
AB BACKGROUND: Tropomyosin from shrimp is the major cross-reacting crustacean food **allergen**. Earlier studies have led to the purification and immunochemical characterization of the major **IgE binding** epitopes of the **allergen**. Maleylated proteins are known to be specifically targeted to scavenger receptors on macrophage. Since antigens processed and presented by macrophages are known to elicit Th1 type of responses and allergic responses are characterized by polarization towards Th2 phenotype, the possibility of modulation of **allergen** -specific immune responses by targeting of tropomyosin to macrophage via scavenger receptor was explored. METHODS: The IgG and **IgE binding** potential of the native maleylated form of tropomyosin was carried out by ELISA and immunoblot. The ability of the native and maleylated form of **allergen** to induce in vitro proliferation of splenocytes from BALB/C mice immunized with both forms of **allergen** was tested. The in vitro production of IL-4 and IFN-gamma by splenocytes from mice immunized with the two forms of **allergen** was determined from culture supernatants. The in vivo production of serum IgG1 and IgG2a antibodies following immunization with native and **modified allergens** was monitored by ELISA. RESULTS: The maleylated form of tropomyosin was found to have reduced antigenicity and allergenicity as compared to its native counterpart. The **modified allergen** was, however, found to elicit a cellular response similar to native tropomyosin in vitro. Analysis of the cytokine profiles showed a modulation from an IL-4-dominant, proallergic, Th2 phenotype to an IFN-gamma-dominant, antiallergic, Th1 phenotype that could also be correlated to a modulation in the in vivo antibody isotype. CONCLUSION: The results suggest the possible potential for modulating allergic responses in vivo by selective targeting to macrophages.

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L19 ANSWER 9 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:259241 The Genuine Article (R) Number: 297YX. Recombinant **allergens**: application to diagnostic and therapeutic perspectives. Pauli G (Reprint); Deviller P. HOP UNIV STRASBOURG, SERV PNEUMOL, BP 426, F-67091 STRASBOURG, FRANCE (Reprint). REVUE DES MALADIES RESPIRATOIRES (FEB 2000) Vol. 17, No. 1BIS, pp. 293-303. Publisher: MASSON EDITEUR. 120 BLVD SAINT-GERMAIN, 75280 PARIS 06, FRANCE. ISSN: 0761-8425. Pub. country: FRANCE. Language: French.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Techniques of generic engineering applied to **allergens** have enabled the production of recombinant **allergens**. The validation of recombinant **allergens** implies that their immunological activity and their identity with natural **allergens** might be confirmed by in vitro and in vivo techniques carried out on a sufficiently large number of allergic subjects. Currently available results for the principal pneumoallergens are reported. Thus the work of validating recombinant **allergen** BeTv1 has been confirmed by in vitro tests and also by skin tests and nasal and bronchial provocation tests. The association of four recombinant **allergens** of phleole has enabled the detection in vitro of sensitisation to germinated pollens in 94.5% of patients. For mites the validity of group 2 recombinant **allergens** has been confirmed. A system enabling the expression of glycosylation of recombinant proteins was necessary to validate recombinant proteins in group 1 **allergens**. The recombinant **allergen** Blot5 is recognised as bring effective in the detection of sensitization to Blomia tropicalis, a domestic **allergen** in sub tropical countries. The recombinant **allergens** Bla g 4 and Bla g 5 have been tested in vitro and in vivo and reactions were positive in nearly 50% of subjects sensitive to cockroaches. The recombinant Asp f 1 has been tested in subjects suffering from allergic bronchopulmonary aspergillosis and is positive in 60-85% of cases.

Some studies are available for recombinant **allergens** of certain animal antigens (Equ c 1, Bos d 2). The consequences of clarifying recombinant **allergens** are then analysed : obtaining better standardised **allergens** for diagnostic tests, studying the spectrum of specificities of IgE induced by an **allergen**, the quantification of specific IgE, a better approach to mixed allergies with the help of recombinant **allergens** of the principal mixed **allergens**. Some recent progress has led to the production of **modified** recombinant **allergens**: the synthesis of recombinant polypeptides corresponding to T epitopes, the production of isoform recombinant **allergens** with reduced allergenic activity, the production of recombinant **allergens** of **modified** allergenic molecules by directed mutations and the production of recombinant fragments of allergenic molecules. The use of **modified** recombinant **allergens** is a way of permitting research which would, in the future, lead to new modalities of specific immunotherapy.

L19 ANSWER 10 OF 49 MEDLINE DUPLICATE 5
2000290931 Document Number: 20290931. PubMed ID: 10828716. Regulation of specific immune responses by chemical and structural modifications of **allergens**. Akdis C A; Blaser K. (Swiss Institute of Allergy and Asthma Research (SIAF), Davos, Switzerland.. akdisac@siaf.unizh.ch) .

INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2000 Apr) 121 (4) 261-9. Ref: 103. Journal code: BJ7; 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB Specific immunotherapy (SIT) is an efficient treatment of allergic diseases to defined **allergens**. Despite being used in clinical practice since early in this century, more rational and safer regimens are required, because SIT is faced with the risk of anaphylaxis and standardization problems of **allergen**-extract-based treatments. A better understanding of the pathogenesis of allergy and of the mechanisms of SIT has led to various approaches to overcome these problems. Knowledge of the influence of IgE-facilitated antigen presentation on **allergen**-specific Th2 responses increased the efforts to generate non-**IgE-binding allergens**. The current principal approach to **allergen** modification is to modify B cell epitopes in order to prevent **IgE binding** and effector cell cross-linking while preserving T cell epitopes to retain the capacity of inducing tolerance. In this way, the **modified allergen** will be directed to T cells by a phagocytosis/pinocytosis-mediated antigen uptake mechanism, bypassing IgE cross-linking and IgE-dependent antigen presentation. Accordingly, a differential regulation of **allergen**-specific T cell cytokine patterns and IgE:IgG production was demonstrated by modifications of the three-dimensional structure of **allergens** because of linearity in T cell epitopes and conformation dependence in B cell epitopes. In this context, chemically **modified allergen** extracts with low **IgE-binding** capacity have been developed to reduce anaphylactic side effects since the early 1980s. The progress of recombinant techniques for producing **allergens** and **allergen** derivatives has led to a dramatic improvement in the ability of developing novel vaccines for the treatment of allergy. This has enabled mutation or deletion of decisive amino acids in B cell epitopes and fractionation or oligomerization of **allergens** by genetic engineering as fruitful approaches to generate hypoallergenic vaccines. Moreover, non-**IgE-binding** short T cell epitope peptides and single-amino-acid-altered peptide ligands represent potential candidates for future SIT.

L19 ANSWER 11 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)

2000:156678 The Genuine Article (R) Number: 285ZF. Post-translational phosphorylation affects the **IgE binding** capacity of caseins. Bernard H (Reprint); Meisel H; Creminon C; Wal J M. CEA, INRA, SPI, LAB IMMUNOALLERGIE ALIMENTAIRE, BATIMENT 136, F-91191 GIF SUR YVETTE, FRANCE (Reprint); CEA SACLAY, SERV PHARMACOL & IMMUNOL, F-91191 GIF SUR YVETTE, FRANCE; BUNDESANSTALT MILCHFORSCH, INST CHEM & PHYS, D-2300 KIEL, GERMANY. FEBS LETTERS (11 FEB 2000) Vol. 467, No. 2-3, pp. 239-244. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS . ISSN: 0014-5793. Pub. country: FRANCE; GERMANY. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB IgE response specific to those molecular regions of casein that contain a major phosphorylation site was analyzed using native and

modified caseins and derived peptides. This study included (i) the naturally occurring common variants A1 and A from beta- and alpha s2-caseins, respectively, which were purified in the native form and then dephosphorylated, (ii) a purified rare variant D of alpha s2-casein which lacks one major phosphorylation site, and (iii) the native and dephosphorylated tryptic fragment f(1-25) from beta-casein. Direct and indirect ELISA using sera from patients allergic to milk showed that the IgE response to caseins is affected by modifying or eliminating the major phosphorylation site. (C) 2000 Federation of European Biochemical Societies.

L19 ANSWER 12 OF 49 CAPLUS COPYRIGHT 2001 ACS
2001:32069 Document No. 134:265170 Large scale production and quality criteria of recombinant **allergens**. Valenta, R.; Twardosz, A.; Vrtala, S.; Kraft, D. (Germany). Arb. Paul-Ehrlich-Inst. (Bundesamt Sera Impfst.) Langen, 93(Regulatory Control and Standardization of Allergenic Extracts), 211-224 (English) 2000. CODEN: APGFEK. ISSN: 0936-8671. Publisher: GIT Verlag GmbH.
AB A review with 74 refs. So far **allergen** exts. used for diagnostic and therapeutic purposes were derived from natural **allergen** sources and consisted of a difficult to standardize mixt. of allergenic and non-allergenic moieties. Standardization and quality control of **allergen** exts. has therefore been limited to biol. evaluation (**IgE binding** capacity, biol. activity) which may give varying results depending on the sensitization profile of individual patients and to antibody-based measurements of a few **allergen** components. Through the application of mol. biol. techniques a continuously increasing no. of recombinant **allergen** mols. has become available for diagnosis and treatment in the last decade.
In contrast to natural **allergen** exts., recombinant **allergens** represent defined mol. identities which can be produced and **modified** according to the intended application by using different vector and host systems as well as by changing the **allergen**-encoding DNA sequences. Here we summarize different strategies for the prodn. of large amts. of recombinant **allergens** and discuss standardization as well as quality criteria useful for the evaluation of recombinant **allergen** mols.

L19 ANSWER 13 OF 49 MEDLINE DUPLICATE 6
2000387444 Document Number: 20347073. PubMed ID: 10887324. Class I chitinases, the panallergens responsible for the latex-fruit syndrome, are induced by ethylene treatment and inactivated by heating. Sanchez-Monge R; Blanco C; Perales A D; Collada C; Carrillo T; Aragoncillo C; Salcedo G. (Unidad de Bioquimica, Departamento de Biotecnologia, E.T.S. Ingenieros Agronomos, Madrid, Spain.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (2000 Jul) 106 (1 Pt 1) 190-5. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB BACKGROUND: Class I chitinases have been identified as the major panallergens in fruits associated with the latex-fruit syndrome, such as avocado, banana, and chestnut. However, other plant foods containing these enzymes have not been related to this syndrome. OBJECTIVE: We sought out class I chitinases in the green bean, a legume that is known to express chitinases but is not associated with latex allergy, and examined whether the content or allergenic activity of chitinases can be **modified**

by physical or chemical treatments. METHODS: **IgE-binding** proteins in untreated bean samples, as well as in ethylene- and heat-treated samples, were detected by using a pool of sera from patients with latex-fruit allergy. Putative **allergens** were purified by cation-exchange chromatography and characterized by N-terminal sequencing, enzymatic activity assays, immunodetection with sera and antichitinase antibodies, and immunoblot inhibition tests. Skin prick tests with untreated and heated purified **allergens** were also carried out. RESULTS: An **IgE-binding** protein of 32 kd that was also recognized by antichitinase antibodies was detected in green bean extracts. This reactive component was strongly induced by ethylene treatment. The protein, designated PvChI, was identified as a class I chitinase closely related to the major avocado **allergen** Prs a 1. Immunoblot inhibition assays demonstrated cross-reactivity between both **allergens**. Purified PvChI induced positive skin prick test responses in 7 of 8 patients with latex-fruit allergy. Heat treatment of both Prs a 1 and PvChI produced a full loss of their allergenic capacities both in vitro and in vivo. No **IgE-binding** component was detected in the white mature bean in which the main isolated 32-kd protein corresponded to a nonreactive phytohemagglutinin. CONCLUSIONS: Ethylene treatment induces the expression of plant class I chitinases. The allergenic activity of plant class I chitinases seems to be lost by heating. This fact could explain why plant foods containing these putative **allergens** that are consumed after cooking are not usually associated with the latex-fruit syndrome.

L19 ANSWER 14 OF 49 MEDLINE DUPLICATE 7
2000385072 Document Number: 20378113. PubMed ID: 10923610.
Identification of allergenic proteins in condoms by immunoenzymatic methods. Docena G H; Benitez P; Fernandez R; Fossati C A. (Catedra de Inmunologia, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, Argentina.. guidoc@biol.unlp.edu.ar) . ANNALS OF ALLERGY, ASTHMA, AND IMMUNOLOGY, (2000 Jul) 85 (1) 77-83. Journal code: CBM; 9503580. ISSN: 1081-1206. Pub. country: United States. Language: English.

AB BACKGROUND: A large increase of allergy to latex proteins has been observed lately probably as a result of a great use of latex-containing goods. At present these untoward reactions have led to consideration of this problem as a health and occupational hazard. It is therefore, . necessary to identify the **allergens** contained in latex-manufactured products and to develop effective diagnostic tools to detect sensitized individuals. OBJECTIVE: The objective of this study is to identify antigenic and allergenic components in latex condoms by using chemical, immunochemical, and immunoenzymatic methods. METHODS: The protein content of extracts obtained from several brands of condoms was determined and characterized by using a **modified** Lowry method, a quantitative ELISA assay and SDS-PAGE. The allergenic behavior of these proteins was studied by IgE immunoblotting, EAST and ELISA techniques, using sera from subjects allergic to latex products, particularly to latex condoms. RESULTS: Wide variations in the protein content (38 to 740 microg/g product) and composition were observed. The SDS-PAGE protein profiles showed components ranging from 7 to 94 kD of relative molecular weights; most of them were also detected in natural rubber latex. The most

prominent bands were revealed in the 14 and 30 kD zones. A strong band of 69 kD in the SDS-PAGE profiles would correspond to a neoantigen, since it was not observed in natural latex. The immunoblotting analysis employing sera from 5 patients allergic to latex condoms showed the presence of 4 components with **IgE binding** capacity (14, 30, 69, and 94 kD). The EAST and ELISA methods showed the presence of **allergens** in all the condom brands studied. CONCLUSIONS: The presence of allergenic proteins in several condom brands was demonstrated by different immunoenzymatic methods.

L19 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2001 ACS
1999:783962 Document No. 132:22180 Compounds binding specifically to Fc.epsilon.RI **IgE binding** sites for pan-specific anti-allergy therapy. Caplan, Michael; Sosin, Howard (USA). PCT Int. Appl. WO 9962550 A1 19991209, 28 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US12526 19990604. PRIORITY: US 1998-90375 19980604.

AB Compns. are administered to block **IgE binding** to receptors and ultimately displace native IgE from mast cells and related cell types, to prevent the activation of these cells during an allergic response. The compns. consist of a pharmaceutically acceptable carrier for systemic or local administration and an amt. of compd. binding specifically to the Fc.epsilon.RI **IgE binding** sites, and more preferably, Fc.epsilon.RI and Fc.epsilon.RII **IgE binding** sites, to prevent activation and degranulation of mast cells in response to exposure to **allergens**. The compds. can consist of IgE mols. and fragments and modifications thereof, such as IgE fragments, humanized or single chain IgE antibodies or fragments thereof, IgE with a **modified** Fab, non-cross-linkable IgE, or peptidomimetics which bind to the same site on the receptor as the IgE, jointly referred to herein as "IgE fragments" unless otherwise stated.

L19 ANSWER 16 OF 49 CAPLUS COPYRIGHT 2001 ACS
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.

AB It has been detd. that **allergens**, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be **modified** to be less allergenic by modifying the **IgE binding** sites. The **IgE binding** sites can be

converted to non-**IgE binding** sites by masking the site with a compd. that prevents **IgE binding** or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the **IgE-binding** epitope, to eliminate **IgE binding**. The method allows the protein to be altered as minimally as possible, other than within the **IgE-binding** sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of **IgE binding** sites. The crit. amino acids within each of the **IgE binding** epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of **IgE binding**. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to **IgE binding**.

L19 ANSWER 17 OF 49 CAPLUS COPYRIGHT 2001 ACS

1999:630793 Document No. 132:150780 Pepsin-digested peanut contains T-cell epitopes but no IgE epitopes. Hong, Soo-Jong; Michael, J. Gabriel; Fehringer, Amy; Leung, Donald Y. M. (Division of Allergy-Immunology, The National Jewish Medical and Research, University of Colorado Health Sciences Center, Denver, CO, 80206, USA). J. Allergy Clin. Immunol., 104(2, Pt. 1), 473-477 (English) 1999. CODEN: JACIBY. ISSN: 0091-6749. Publisher: Mosby, Inc..

AB Peanuts are a common cause of food-induced anaphylaxis and fatalities. Previous studies have demonstrated that rush immunotherapy to crude peanut ext. reduces clin. symptoms triggered by oral peanut challenges, but the immunotherapy was assocd. with an unacceptably high incidence of systemic allergic reactions. One approach to reduce the frequency of allergic reactions would be to use a **modified** peanut antigen with low allergenic properties. The authors sought to det. the immunol. characteristics of crude intact peanut ext. before and after pepsin digestion by using IgE immunoblotting and assessment of T-lymphocyte responses to intact and peptic digests of peanut exts. Western blot anal. of sera from 5 subjects with peanut allergy showed multiple IgE-reactive proteins in crude intact peanut ext. that were eliminated after pepsin treatment of the peanut ext. In contrast, pepsin-digested peanut induced significant T-cell proliferation responses (stimulation index = 30) in vitro in PBMCs from 7 subjects with peanut allergy, albeit at lower levels than that induced by intact peanut (stimulation index = 66). Furthermore, IFN-.gamma. prodn. was induced by intact peanut and pepsin-digested peanut in a concn.-dependent manner. Importantly, T-cell lines generated in response to intact peanut also reacted to pepsin-digested peanut, indicating cross-reactive T-cell epitopes in intact and pepsin-digested peanut. These findings suggest that pepsin-digested peanut may be useful in peanut immunotherapy because pepsin digestion eliminates IgE reactivity but maintains T-cell reactivity.

L19 ANSWER 18 OF 49 MEDLINE DUPLICATE 8

2000039787 Document Number: 20039787. PubMed ID: 10574630. Mapping of **IgE binding** regions in the major rat urinary protein, alpha 2u-globulin, using overlapping peptides. Bayard C; Siddique A B; Berzins K; Troye-Blomberg M; Hellman U; Vesterberg O. (Department of Occupational Medicine, National Institute for Working Life, Solna, Sweden.. bayard@niwl.se) . IMMUNOLOGICAL INVESTIGATIONS, (1999 Sep-Dec) 28 (5-6) 323-38. Journal code: GI5; 8504629. ISSN: 0882-0139. Pub. country: United States. Language: English.

AB Exposure to laboratory animals poses a hazard for development of occupational allergy. Identification of antigenic determinants of allergenic proteins may be valuable for immunotherapeutic purposes. Overlapping peptides of the major **allergen** in rat urine, Rat n 1.02, corresponding to the protein alpha2u-globulin were synthesised on solid support and screened simultaneously to locate **IgE binding** linear epitopes using a simple **modified** ELISA procedure. Thirty-nine peptides were synthesised, each 8 amino acids long with 4 amino acids overlaps. Sera from fifteen rat-sensitized subjects were analyzed and as controls sera from 7 non-rat-sensitized individuals were used. In general low binding and a great individual variation between sera from rat allergic individuals were seen. Some peptides were more frequently recognized by IgE antibodies in sera from rat allergics. These peptides were mainly clustered towards the N-terminal and C-terminal parts of the protein. Taken together our data suggest the existence of linear **IgE binding** epitopes in the rat urine **allergen** , Rat n 1.02. However, the role of these sequences in the allergic reaction needs further investigation.

L19 ANSWER 19 OF 49 MEDLINE DUPLICATE 9

1999242424 Document Number: 99242424. PubMed ID: 10224369. The importance of recombinant **allergens** for diagnosis and therapy of IgE-mediated allergies. Kraft D; Ferreira F; Vrtala S; Breiteneder H; Ebner C; Valenta R; Susani M; Breitenbach M; Scheiner O. (Institute of General and Experimental Pathology, University of Vienna, Austria.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1999 Feb-Apr) 118 (2-4) 171-6. Journal code: BJ7; 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB In the past 10 years, a considerable number of cDNAs coding for **allergens** have been isolated and expressed. Intensive investigations showed that recombinant **allergens** and their respective natural counterparts possess comparable properties with respect to structure, function and interaction with the immune system. Recent studies documented that in vitro as well as in vivo diagnosis of IgE-mediated allergic diseases can be successfully improved by the application of recombinant **allergens**. In addition, new strategies for a safer specific immunotherapy (SIT) have been developed based on the knowledge of the primary structures of **allergens**. Naturally occurring isoforms of **allergens** as well as recombinant **allergens** with **modified** amino acid sequences show very low **IgE binding** capacity but strong T cell-stimulatory activity and represent possible candidates. In case of Bet v 1, the major birch pollen **allergen**, isoforms d, g and l and a Bet v 1a mutant, produced by site-directed mutagenesis resulting in 6 amino acid

exchanges, fulfilled the above mentioned criteria. In a third approach, two adjacent peptides covering the entire Bet v 1a sequence were produced in an Escherichia coli expression system. These peptides contained most of the relevant T cell epitopes, but lost their **IgE binding** capacity and, thus, their ability to activate mast cells and basophils of sensitized patients. Our results suggest that **allergen** variants (isoforms, mutants, T cell epitope-containing peptides) may be used as 'hypoallergenic agents' in SIT.

L19 ANSWER 20 OF 49 MEDLINE DUPLICATE 10
1999236624 Document Number: 99236624. PubMed ID: 10221435.
Physicochemical and immunologic characterization of low-molecular-weight allergoids of Dactylis glomerata pollen proteins. Cirkovic T D; Bukilica M N; Gavrovic M D; Vujcic Z M; Petrovic S; Jankov R M. (Faculty of Chemistry, Belgrade, Yugoslavia.) ALLERGY, (1999 Feb) 54 (2) 128-34. Journal code: 39C; 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB BACKGROUND: Orchard grass (Dactylis glomerata) pollen proteins were chemically **modified** by means of acid anhydrides (maleic and succinic anhydride) to obtain low-molecular-weight allergoids. Chemical modification in both cases led to the replacement of one positive charge (epsilon amino group of Lys) by one negative charge, yielding proteins with changed physicochemical properties in comparison to the native orchard grass-pollen proteins. METHODS: Physicochemical characterization of derivatives was done by gel chromatography, SDS-PAGE, and isoelectric focusing. To examine the **IgE-binding** properties of these derivatives, we carried out immunoblotting. To examine the ability of derivatives to induce IgG production, we immunized rabbits. Skin prick testing with the allergoids was performed on 15 individuals allergic to orchard grass pollens and on two healthy subjects. RESULTS: It was shown that the **modified** proteins retain their original molecular weights, but change pI to more acidic values. In the case of allergoids, a strong reduction in **IgE binding** was found. Immunization of rabbits with allergoids showed that the derivatives retain the ability to induce IgG production, and that the antisera obtained in such a way react to native (unmodified) extract. The ability of derivatives to induce allergic reaction was significantly reduced. The patients (86.6%) included in our study exhibited less than 50% of native extract response. Among them, 53.3% had no response to one or both allergoids. CONCLUSIONS: These modification procedures yield allergoids with a reduced allergenic activity and preserved immunogenic potential suitable for use in immunotherapy.

L19 ANSWER 21 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:544997 The Genuine Article (R) Number: 214EK. Genetically engineered plant **allergens** with reduced anaphylactic activity. Singh M B (Reprint); deWeerd N; Bhalla P L. UNIV MELBOURNE, INST LAND & FOOD RESOURCES, PLANT MOL BIOL & BIOTECHNOL LAB, PARKVILLE, VIC 3052, AUSTRALIA (Reprint). INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (JUN 1999) Vol. 119, No. 2, pp. 75-85. Publisher: KARGER. ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. ISSN: 1018-2438. Pub. country: AUSTRALIA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Allergy immunotherapy is based on the administration of increasing amounts of the disease-eliciting **allergens** in order to yield **allergen**-specific non-responsiveness. Success of this therapy is associated with modulation of the immune response to allergenic molecules at the level of T-helper cells and the induction of blocking antibodies. The extracts used for immunotherapy are highly heterogenous preparations from natural sources and contain additional components, mostly proteins which are not well defined, Recombinant DNA technology offers novel tools for production of pure and well-characterised **allergens** for specific immunotherapy. However, high IgE reactivity of pure recombinant **allergens** is associated with an increased risk of potentially life-threatening anaphylactic reactions. A major improvement in **allergen**-specific immunotherapy may be achieved by using genetically engineered recombinant **allergens** with reduced anaphylactic activity. Recently the site-directed mutagenesis technique has been applied successfully to produce variants of major grass, birch and oilseed rape **allergens** with reduced IgE reactivity but retained T-cell reactivity. These **modified allergens** with reduced anaphylactic potential are novel candidates for safer and more effective **allergen**-specific immunotherapy.

L19 ANSWER 22 OF 49 CAPLUS COPYRIGHT 2001 ACS
1998:682138 Document No. 129:301697 Mutants of grass **allergens** not recognized by IgE of allergic patients and their use in specific immunotherapy. Kahlert, Helga; Stuwe, Hans-Thomas; Fiebig, Helmut; Cromwell, Oliver; Becker, Wolf-Meinhard; Bufe, Albrecht; Schramm, Gabriele; Jager, Lothar; Muller, Wolf-Dieter (Merck Patent G.m.b.H., Germany). PCT Int. Appl. WO 9843657 A2 19981008, 58 pp. DESIGNATED STATES: W: HU, JP, PL, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (German). CODEN: PIXXD2. APPLICATION: WO 1998-EP1507 19980316. PRIORITY: DE 1997-19713001 19970327.
AB Mutants of **allergens** of a grass (Phleum pratense) that stimulate the lymphocyte proliferation and cytokine synthesis in sufferers of pollen allergies, but have significantly lower binding to serum IgE antibodies of patients are described. The **allergens** can be manufd. by expression of the cloned gene for use in immunotherapy of grass allergies. Specifically, the T-cell epitopes of the **allergens** are **modified** and the modification may arise from a spontaneous mutation or by site-specific mutagenesis. T cell epitopes of the Phl p 5 **allergen** were identified and **allergen** derivs. lacking the most significant ones were prepd. by site-directed mutagenesis involving amino acid substitutions and deletions. The derivs. showed very little **allergen** activity as judged by their inability to inhibit **IgE binding** to wild-type **allergen**.

L19 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2001 ACS
1998:774558 Document No. 130:36961 Molecular medical science of **allergens**. Okumura, Yasushi (Biosci. Res. Dev. Lab., Asahi Brew., Ltd., Ibaraki, 302-01, Japan). Saishin Igaku, 53(12), 2824-2829 (Japanese) 1998. CODEN: SAIGAK. ISSN: 0370-8241. Publisher: Saishin Igakusha.
AB A review with 11 refs., on cloning of mite **allergen** Der f2 gene, detn. and conformation anal. of **IgE binding** site of Der f2, and utility of **modified** Der f2 as a hyposensitizer for

allergy immunotherapy.

L19 ANSWER 24 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:48419 The Genuine Article (R) Number: 153FG. Mapping of T-cell epitopes of Phl p 5: evidence for crossreacting and non-crossreacting T-cell epitopes within Phl p 5 isoallergens. Muller W D (Reprint); Karamfilov T;
Kahlert H; Stuwe H T; Fahlbusch B; Cromwell O; Fiebig H; Jager L. UNIV JENA, INST CLIN IMMUNOL, JOHANNISFRIEDHOF 3, D-07743 JENA, GERMANY (Reprint); ALLERGOPHARMA J GANZER KG, REINBEK, GERMANY. CLINICAL AND EXPERIMENTAL ALLERGY (DEC 1998) Vol. 28, No. 12, pp. 1538-1548.
Publisher:
BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0954-7894. Pub. country: GERMANY. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background Group 5 **allergens** represent major grass pollen **allergens** because of their high sensitization indices. The identification of T-cell epitopes of these **allergens** is a prerequisite for the design of immunotherapeutic strategies based on peptide vaccination or **modified allergens** with conserved T-cell epitopes.

Objective This study was undertaken to determine T-cell epitopes on Phl p 5 major pollen **allergen** of timothy grass (Phleum pratense).

Methods T-cell lines (TCLs) and T-cell. clones (TCCs), specific to Phl p 5, were established from the peripheral blood of 18 patients allergic to grass pollen. All TCCs were mapped for epitope specificities using 178 overlapping dodecapeptides representing the primary structures of two isoforms of Phl p 5 (Phl p 5a and Phl p 5b). Phenotype and cytokine production profiles of TCCs were tested. Selected TCCs were analysed for HLA class II restriction.

Results A total of 82 TCCs were isolated. All TCCs displayed the helper cell (TH) phenotype. Their reactivity with two recombinant expressed isoforms of Phl p 5a and Phl p 5b was heterogeneous. The epitope specificity of the TCCs was then revealed. Nineteen T-cell epitopes could be identified on Phl p 5. Eighty-one percent of mapped TCCs recognized three T-cell reactive regions on the Phl p 5 **allergen**. Some TCCs were reactive with isoepitopes presenting on Phl p 5a as well as Phl p 5b. **Allergen**-specific stimulation induced a TH0-like type of cytokine production in 25 of 50 TCCs. Almost all TCCs secreted high concentrations of interleukin-13.

Conclusion Phl p 5, a major grass pollen **allergen**, contains several T-cell epitopes. Some epitope regions were recognized by several patients. Epitope recognition pattern could not be correlated with special HLA class II haplotypes. T-cell stimulating isoepitopes were found at corresponding regions of Phl p 5a and Phl p 5b isoforms.

L19 ANSWER 25 OF 49 MEDLINE DUPLICATE 11
1998202081 Document Number: 98202081. PubMed ID: 9543081.
Post-translational modifications influence IgE reactivity to the major **allergen** Phl p 1 of timothy grass pollen. Petersen A; Schramm G; Schlaak M; Becker W M. (Forschungszentrum Borstel, Biochemical and Molecular Allergology, Germany.) CLINICAL AND EXPERIMENTAL ALLERGY, (1998

Mar) 28 (3) 315-21. Journal code: CEB; 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: Grass group I consists of very potent allergenic components which are found in the pollen of all temperate grasses. Several post-translational modifications are predicted from the cDNA data. OBJECTIVE: The aim of this study was to identify sequential **IgE-binding** sites on the **allergen** Phl p 1 and to determine their influence on IgE reactivity. METHODS: Based on cDNA data and microsequencing results we synthesized overlapping decapeptides covering the complete Phl p 1 molecule and tested them for immunological reactivity by means of the PEPSCAN technique. In a dot test we determined the frequency of IgE reactivities to post-translationally **modified** structures (hydroxylated proline residues, carbohydrate structure, and disulphide formations). RESULTS: Screening by overlapping peptides demonstrated an **IgE binding** site on the 10 N-terminal amino acids. Comprehensive studies showed that the two hydroxyproline residues of the native Phl p 1 **allergen** (at positions 5 and 8) and the N-glycan (at position 9) can result in an increased IgE reactivity; 3.3% of the sera exclusively bound to the hydroxyproline bearing peptide, while only 0.4% bound to the proline containing peptide. With regard to glycosylation, we estimated that 20% of sera recognized protein and carbohydrate epitopes, while one serum exclusively bound to the glycan. The formation of disulphide bonds has no detectable effect on the IgE reactivity to Phl p 1. CONCLUSION: Our results indicate that the post-translational modifications, the carbohydrate structure and the hydroxylation of proline residues, can enhance the IgE reactivity of Phl p 1.

L19 ANSWER 26 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)

1999:112329 The Genuine Article (R) Number: 162DN. Novel food products from genetically **modified** crop plants: methods and future prospects. Dunwell J M (Reprint). UNIV READING, SCH PLANT SCI, READING, BERKS, ENGLAND (Reprint). INTERNATIONAL JOURNAL OF FOOD SCIENCE AND TECHNOLOGY (JUN 1998) Vol. 33, No. 3, pp. 205-213. Publisher: BLACKWELL SCIENCE LTD.

P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0950-5423. Pub. country: ENGLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Using a variety of in vitro techniques, it is now possible to isolate a selected gene sequence from any source and introduce it into any major crop plant. Millions of hectares of such genetically **modified** (GM) or transgenic plants are already being grown commercially, mostly in North America. To date, the most widely grown GM crops (soybean and maize) are those with **modified** agronomic traits (herbicide or insect tolerance); the products from these commodity crops are now included in a wide range of processed foods. This review describes the methods used to generate these Gh I crops and then discusses the range of **modified** food products that can be generated using this new technology. Such products include those with altered protein, starch or oil quality, as well as examples of improved micronutrient or vitamin content. Much of this work, particularly that aiming to develop food with specific health benefits, is still at the experimental stage, but there is no doubt that many GM foodstuffs, with an increasing variety of qualitative changes, will reach the market in the coming years. The rate at which such products

are developed commercially depends to a large extent on the public reaction to a technology still poorly understood by most consumers.

L19 ANSWER 27 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)
1998:104721 The Genuine Article (R) Number: YT529. Diagnostic value of recombinant **allergens**.. Pauli G (Reprint). HOP UNIV STRASBOURG, SERV PNEUMOL, BP 426, F-67091 STRASBOURG, FRANCE (Reprint). REVUE FRANCAISE D ALLERGOLOGIE ET D IMMUNOLOGIE CLINIQUE (JAN 1997) Vol. 37, No.
8, pp. 1093-1101. Publisher: EXPANSION SCI FRANCAISE. 31 BLVD LATOUR MAUBOURG, 75007 PARIS, FRANCE. ISSN: 0335-7457. Pub. country: FRANCE. Language: French.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Genetic engineering techniques applied to **allergens** have allowed the production of recombinant **allergens**. Validation of recombinant **allergens** demands confirmation of their immunological activity and their identity with natural **allergens** by in vivo and in vitro techniques on a sufficiently large number of allergic subjects. The results currently available for the main respiratory **allergens** ar reported. For example, the validity of the birch recombinant **allergen** Bet v 1 was confirmed by in vitro tests, but also by skin tests and nasal and bronchial challenge tests. The
combination of four recombinant **allergens** of timothy allowed the in vitro detection of sensitization to Graminaceae pollens in 94.5% of patients. The validity of up 2 recombinant **allergens** has been confirmed for house dust mites. Systems of expression allowing glycosylation of recombinant proteins were necessary to validate group 1 recombinant **allergen** proteins. Recombinant **allergen** Blo t 5 has been tested in vitro and in vivo, and was found to be effective in the detection of sensitization to Blomia tropicalis, a domestic **allergen** in subtropical countries. Only recombinant **allergen** Bla g 4 has been tested in vitro and in vivo, with positive reactions in almost 50% of subjects sensitized to crockroaches. Recombinant Asp f 1 was tested in subjects suffering from allergic bronchopulmonary aspergillosis, and was positive in 60 to 85% of cases. Studies are also available for recombinant **allergens** of phospholipase A2, the major **allergen** of bee venom. The consequences of the development of recombinant **allergens** are then analysed: better standardized **allergens** for diagnostic tests, study of the spectrum of specificities of the IgE induced by an **allergen**, quantification of specific IgE, better approach to cross-allergies using recombinant **allergens** of the main cross **allergens**. The application of recombinant **allergens** to basic research has led to production of **modified** recombinant **allergens**: synthetis of recombinant polypeptides corresponding to T epitopes, production of recombinant **allergens** isoforms with reduced allergenic activity, production of recombinant **allergens** of allergenic molecules **modified** by directed mutations. The use of these **modified** recombinant **allergens** is one line of research which, in the future, may lead to new modalities of specific desensitization. Other lines of research are also under investigation: inhibition of antigen-antibody reactions by the use of recombinant Fab-blocking molecules, and recombinant molecules: of immunodominant haptens.

L19 ANSWER 28 OF 49 MEDLINE DUPLICATE 12
97351910 Document Number: 97351910. PubMed ID: 9208192. Purification and

IgE binding capacity of Der s 3, a major **allergen** from Dermatophagoides siboney. Ferrandiz R; Casas R; Dreborg S. (Department of Paediatrics, Linkoping University Hospital, Sweden.) CLINICAL AND EXPERIMENTAL ALLERGY, (1997 Jun) 27 (6) 700-4. Journal code: CEB; 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: Sensitization to the house dust mite Dermatophagoides siboney has been demonstrated in asthmatic patients. Previously, Dermatophagoides siboney group 1 and group 2 **allergens**, named Der s 1 and Der s 2, respectively, have been purified. OBJECTIVES: The aim of this study was to purify and to study the IgE reactivity of 30 kDa component, suspected to correspond to group 3 **allergens**. METHODS: The protein was purified by affinity chromatography using anti-Der f 3 monoclonal antibodies and semi-preparative SDS-PAGE. The **IgE binding** capacity of the purified fractions was tested with sera from 106 mite-sensitive asthmatic patients using a **modified** chemiluminiscent method. RESULTS: Affinity chromatography resulted in fractions containing the 30 kDa component which was further purified to homogeneity by SDS-PAGE. Seventy-three per cent of the sera showed IgE reactivity to this protein, indicating that it is a major **allergen**. The protein also reacted with anti Der f 3 polyclonal antibodies and had tryptic activity. There were differences in the reactivity to Der s 3 according to the age of the patients. CONCLUSION: Based on the frequency of IgE reactions and the reactivity with antibodies directed to Der f 3, it is proposed to name this 30 kDa **allergen** from D. siboney, Der s 3.

L19 ANSWER 29 OF 49 MEDLINE DUPLICATE 13

97414840 Document Number: 97414840. PubMed ID: 9269506. Preseasonal specific immunotherapy with **modified** Phleum pratense allergenic extracts: tolerability and effects. Ricca V; Ciprandi G; Pesce G; Riccio A; Varese P; Pecora S; Canonica G W. (Servizio di Allergologia, Ospedale Koelliker de Missionari di Maria S.S. Consolata, Torino, Italia.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1997 Jul-Aug) 25 (4) 167-75. Journal code: 3AH; 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB The preparation of chemically **modified allergens**, with a reduced **IgE binding** capacity (responsible for side effects with traditional immunotherapy) but with the same or greater immunogenic activity, is one of the paths followed to obtain better results with specific immunotherapy (IT). The aim of the study was to evaluate the tolerability and effects of an extract Phleum pratense, **modified** with glutaraldehyde and absorbed on aluminium hydroxide, in controlling the seasonal symptomatology induced by grass pollen in a group of 10 monosensitized patients, compared to a group of 10 similar patients not treated with specific IT but with drugs alone. The monitoring parameters were: 1) Clinical: a) symptomatology after specific conjunctival provocation test (pre and post seasonal) and during the natural exposure to the **allergen** b) drug consumption. 2) Immunological (peripheral blood eosinophils, total and specific IgE, total specific IgG). 3) Cytological, before, during and after the pollen season. CONCLUSIONS: In subjects treated with specific IT a) both the overall

symptomatology and the drug consumption resulted significantly reduced compared to the controls (p = 0.045); b) the phlogistic infiltrate showed a tendency to decrease during the pollen season; c) the peripheral blood eosinophils, total and specific IgE and IgG did not show any significant variation compared to the controls; d) no systemic reactions occurred and there were only two slight local reactions.

L19 ANSWER 30 OF 49 CAPLUS COPYRIGHT 2001 ACS
1997:185279 Document No. 126:249934 Expression, purification and immunochemical characterization of recombinant bovine beta-lactoglobulin, a major cow milk **allergen**. Chatel, Jean-Marc; Bernard, Herve; Clement, Gilles; Frobert, Yveline; Batt, Carl A.; Gavalchin, Jerrie; Peltre, Gabriel; Wal, Jean-Michel (INRA-CEA, DRM-SPI, Gif Sur Yvette, 91191, Fr.). Mol. Immunol., 33(14), 1113-1118 (English) 1996. CODEN: MOIMD5. ISSN: 0161-5890. Publisher: Elsevier.
AB The immunol. characteristics of a recombinant beta-lactoglobulin were studied using monoclonal antibodies, polyclonal antiserum and sera from allergic patients. Recombinant beta-lactoglobulin (rBLG) was expressed in Escherichia coli strain DH5.alpha. and purified, as previously described. The method has been **modified** by adding an immunoaffinity purifn. step. A quantity of 5-10 mg of purified rBLG per L of medium culture can be produced rBLG shared the same mol. wt. as the natural BLG (nBLG) and also possessed at least one intrachain disulfide bridge. In HPLC, rBLG appeared as a single peak, and the purity was estd. to be greater than 95%. All the monoclonal antibodies (mAbs) used in this study recognized different epitopes of the BLG and presented compatible binding. No differences could be detected between rBLG and nBLG when tested in a Western blot with rabbit polyclonal antiserum or with three mAbs that bound preferentially the reduced and S-carboxymethylated form of BLG. In a competitive enzyme immunoassay (EIA) using either a rabbit polyclonal antiserum or four mAbs that recognized conformational epitopes, we could not distinguish between rBLG or nBLG. In direct ELISA using nBLG or rBLG as the immobilized **allergen**, we measured a similar concn. of specific anti-BLG IgE in five sera from allergic patients. The results of this study indicate that we have obtained a rBLG with biochem. and immunol. properties very similar to nBLG.

L19 ANSWER 31 OF 49 MEDLINE DUPLICATE 14
97163754 Document Number: 97163754. PubMed ID: 9010561. Preseasonal specific immunotherapy with **modified** phleum pratense allergenic extracts: tolerability and effects. Vittorio R; Giorgio C; Giampaola G; Annamaria R; Paola V; Silvia P; Walter C G. (Servizio di allergologia, ospedale koelliker dei missionari di Maria S.S. Consolata, Torino, Italia.
) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1996 Nov-Dec) 24 (6) 255-62. Journal code: 3AH; 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.
AB The preparation of chemically **modified allergens**, with a reduced **IgE binding** capacity (responsible for side effects with traditional immunotherapy) but with the same or greater immunogenic activity, is one of the paths followed to obtain better results with specific immunotherapy (IT). The aim of the study was to evaluate the tolerability and effects of extracts of Phleum pratense, **modified** with glutaraldehyde and absorbed on aluminium hydroxide, in controlling the seasonal symptomatology induced by grass pollen in a

group of 10 monosensitized patients, compared to a group of 10 similar patients not treated with specific IT but with drugs alone. The monitoring parameters were: 1) Clinical: a) symptomatology after specific conjuctival provocation test (pre and post seasonal) and during the natural exposure to the **allergen** b) drug consumption. 2) Immunological (peripheral blood eosinophils, total and specific IgE, total specific IgG). 3) Cytological, before, during and after the pollen season. Conclusions: in subjects treated with specific IT a) both the overall symptomatology and the drug consumption resulted significantly reduced compared to the controls ($p = 0.045$); b) the phlogistic infiltrate showed a tendency to decrease during the pollen season; c) the peripheral blood eosinophils, total and specific IgE and IgG did not show any significant variation compared to the controls; d) no systemic reactions occurred and there were only two slight local reactions.

L19 ANSWER 32 OF 49 CAPLUS COPYRIGHT 2001 ACS
1995:680795 Document No. 123:81614 Recombinant preparation of **modified allergen** Der fII as antiallergic agents. Nishama, Chiharu; Juki, Toshifumi; Okumura, Yasushi; Shibuya, Ichiro (Asahi Breweries Ltd, Japan; Torii Yakuhin Kk; Nikka Whisky). Jpn. Kokai Tokkyo Koho JP 07095887 A2 19950411 Heisei, 50 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1993-275897 19930929.
AB **Allergen** Der fII of Dermatophagoides farinae is **modified** by replacing certain residues with Ala to lower its **IgE-binding** activities. The **modified allergen** can be produced by expressing its coding gene in an eukaryotic host and used as an antiallergic agent.

L19 ANSWER 33 OF 49 CAPLUS COPYRIGHT 2001 ACS
1995:412684 Document No. 122:212100 Recombinant preparation of **allergen** Der f II muteins of Dermatophagoides farinae with lowered **IgE-binding** activity. Takai, Toshiro; Juki, Toshifumi; Okumura, Yasushi; Yamakawa, Hiroshi; Ando, Tooru; Hirai, Mitsuo (Asahi Breweries Ltd, Japan; Torii Yakuhin Kk; Nikka Whisky). Jpn. Kokai Tokkyo Koho JP 06253851 A2 19940913 Heisei, 13 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1993-139793 19930304.
AB **Allergen** Der f II of Dermatophagoides farinae is **modified** by site-specific mutation to obtain a mutein with lowered **IgE-binding** activity. 1 Or 2 of Cys of positions 8, 21, 27, 73, 78, and 119 are replaced by Ser with this method. These muteins can be used for treating the diseases assocd. with Dermatophagoides farinae **allergens**.

L19 ANSWER 34 OF 49 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 15
94305698 EMBASE Document No.: 1994305698. [Clinical and experimental trends in hyposensitization]. KLINISCHE UND EXPERIMENTELLE TRENDS DER HYPOSENSIBILISIERUNG. Jager L.. Humboldtstrasse 3,D-07740 Jena, Germany. Allergologie 17/9 (400-403) 1994.
ISSN: 0344-5062. CODEN: ALLRDI. Pub. Country: Germany. Language: German. Summary Language: German; English.
AB Hyposensitization has been developed starting from a wrong idea. Only during the last 15 years methods for an exact analysis of the underlying mechanisms became available - especially due to the progress in immunology. The first step was the characterization and purification of **allergens** from natural sources. The next one was the identification of **IgE-binding** epitopes. At present

research activities are concentrated on T cell epitopes. By their means, above all, a modulation of the immune response could be achieved. This will be the scientifically-based way to the development of **modified allergen**.

L19 ANSWER 35 OF 49 CAPLUS COPYRIGHT 2001 ACS
1995:298531 Document No. 123:31159 **Modified** par j I **allergen** from P. judaica pollen and its rate of absorption in rats. [Erratum to document cited in CA121:132140]. Mistrello, G.; Roncarolo, D.; Gentili, M.; Zanoni, D.; Falagiani, P. (Research Department, Laboratorio Farmaceutico Lofarma, Milano, 20143, Italy). Immunol. Lett., 41(2-3), 291 (English) 1994. CODEN: IMLED6. ISSN: 0165-2478.
AB The errors were not reflected in the abstr. or the index entries.

L19 ANSWER 36 OF 49 MEDLINE DUPLICATE 16
95012426 Document Number: 95012426. PubMed ID: 7927511. **Modified** par j I **allergen** from P judaica pollen and its rate of absorption in rats. Mistrello G; Roncarolo D; Gentili M; Zanoni D; Falagiani P. (Research Department, Laboratorio Farmaceutico Lofarma, Milano, Italy.) IMMUNOLOGY LETTERS, (1994 Apr) 40 (1) 31-6. Journal code: GIH; 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.
AB Polymerized **allergens** (allergoids) have been introduced in the immunotherapy of allergic disease in order to reduce the risk of side effects. However, their high molecular weight can be a limit, particularly when they are administered by a route involving passage through the mucosal barrier. We describe a simple procedure aimed at developing an original **modified allergen** with significantly less allergenic potential (intended as human **IgE-binding** capacity) but preserving the monomeric nature of the molecule. Par j I, the major **allergen** of Parietaria judaica pollen, was purified by a combination of monoclonal antibodies and affinity chromatography. Par j I **allergen** was then **modified** by reaction with potassium cyanate (KCNO), and compared with the native **allergen** to evaluate its allergenic potency (RAST-inhibition) and molecular weight (SDS-PAGE). **Modified allergen** showed significantly lower allergenic potency but kept its original molecular weight, making it particularly suitable for buccal (sublingual) administration. To study the adsorption profile, **modified** Par j I was radiolabeled and administered intravenously and sublingually to normal rats. The prospects for clinical application of the **modified allergen** are discussed.

L19 ANSWER 37 OF 49 CAPLUS COPYRIGHT 2001 ACS
1992:632043 Document No. 117:232043 Improved preparation of cat dander **allergens** for immunotherapeutic purposes and uses therefor. Kuo, Mei Chang; Bond, Julian (Immulogic Pharmaceutical Corp., USA). PCT Int. Appl. WO 9215613 A1 19920917, 36 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US1344 19920220. PRIORITY: US 1991-662193 19910228.
AB **Modified** human T-cell-reactive feline protein (TRFP), for use in place of cat dander ext. for desensitization treatment of individuals allergic to cats, has a substantially unaltered ability to stimulate

T-cells from such individuals but a reduced ability to bind IgE from these individuals. Affinity-purified TRFP is **modified** by treatment with mild alkali to remove O-linked carbohydrate moieties; **modified** TRFP may also be produced by recombinant DNA technol. Thus, TRFP was treated with KOH at pH 12.5 and room temp. for 16 h to inhibit **IgE binding** totally in immunoblot expts. and to inhibit histamine-releasing activity 100-fold.

L19 ANSWER 38 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)
92:623081 The Genuine Article (R) Number: JU254. THE ANTIGENICITY AND ALLERGENICITY OF MICROPARTICULATED PROTEINS - SIMPLESSE(R). SAMPSON H A (Reprint); COOKE S. JOHNS HOPKINS UNIV, DEPT PEDIAT, DIV ALLERGY IMMUNOL, BALTIMORE, MD, 21218. CLINICAL AND EXPERIMENTAL ALLERGY (OCT 1992) Vol. 22, No. 10, pp. 963-969. ISSN: 0954-7894. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB New technologies are allowing the food industry to develop products from standard foods which may not be recognized in its **modified** form by food allergic patients. One such product, Simplesse(R), has been formulated by microparticulation of egg white and/or cows' milk proteins and is used as a fat substitute in many fat-laden foods. The purpose of this study was to determine whether the process of microparticulation altered the allergenicity/antigenicity of egg white and cows' milk proteins compared to the starting materials.

Soluble protein fractions of Simplesse(R) and its respective starting materials were compared to egg white, cows' milk protein, an ultra-filtered egg white/condensed milk mixture, and/or a whey concentrate by SDS-polyacrylamide gel electrophoresis. In addition, sera from 16 patients with documented egg and/or cows' milk hypersensitivity and two controls who were not allergic to egg or milk were used to assess potential allergenicity/antigenicity of these products by immunoblot (Western blot) analysis. There were heterogeneous IgE and IgG binding patterns to the food fractions among these food allergic patients suggesting differing sensitivity patterns among the individuals tested. However, utilizing both SDS-PAGE and immunoblot analyses, the major **allergens** in the microparticulated products were the same as those found in the starting materials, egg and cows' milk. In addition, there was no evidence of 'novel' protein fractions in the Simplesse(R) test materials compared to the starting materials.

L19 ANSWER 39 OF 49 MEDLINE DUPLICATE 17
92306006 Document Number: 92306006. PubMed ID: 1611548. Group V **allergens** in grass pollens: IV. Similarities in amino acid compositions and NH2-terminal sequences of the group V **allergens** from Lolium perenne, Poa pratensis and Dactylis glomerata. Klysner S; Welinder K G; Lowenstein H; Matthiesen F. (ALK Research, Horsholm, Denmark.) CLINICAL AND EXPERIMENTAL ALLERGY, (1992 Apr) 22 (4) 491-7. Journal code: CEB; 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Monoclonal antibodies (PpV4) raised against Phleum pratense group V **allergen** were used for immuno-affinity chromatography of cross-reacting group V **allergens** from related grass species. Fractions enriched in group V **allergen** were obtained from Lolium perenne, Poa pratense and Dactylis glomerata extracts. The major components in these fractions were found in the Mwr range 25-28 kD.

IgE binding to these components was shown using a pool of grass allergic sera, by SDS-PAGE immunoblotting. These fractions were electroblotted from tricine SDS-PAGE gels onto a polyvinylidene-difluoride membrane and selected group V bands were directly cut out and used for amino acid analysis and NH2-terminal sequencing. Both the amino acid compositions and the NH2-terminal sequences obtained for each group V **allergen** were almost similar to each other and to the sequence and composition of the previously described **allergen** Phl p V from Phleum pratense. A common trait of the investigated **allergens**, is the very high contents of alanine (25-32%) and the presence of the **modified** amino acid, hydroxyproline.

L19 ANSWER 40 OF 49 CAPLUS COPYRIGHT 2001 ACS
1994:432588 Document No. 121:32588 Mapping of **allergen** epitopes by antibodies. Aalberse, R. C. (Cent. Lab. the Neth. Red Cross Blood Transfus. Serv., Amsterdam, 1066, Neth.). Adv. Allergol. Clin. Immunol., Proc. Eur. Congr., 15th, 103-7. Editor(s): Godard, Philippe; Bousquet, Jean; Michel, Francois-Bernard. Parthenon Publ. Group: Carnforth, UK. (English) 1992. CODEN: 59YQAO.

AB A review with 3 refs. discussing the specificity of IgE antibodies, why epitope mapping is of interest, procedures for mapping **IgE-binding** epitopes on **allergens**, inhibition by monoclonal anti-**allergen** antibodies, phylogenetic **allergen** variants, chem. or enzymically **modified allergens**, variant **allergens** prepd. by rDNA technol., and synthetic peptides.

L19 ANSWER 41 OF 49 MEDLINE DUPLICATE 18
92180958 Document Number: 92180958. PubMed ID: 1796777. Analysis of allergenic components of Bermuda grass pollen by monoclonal antibodies. Chang Z N; Tsai L C; Chi C W; Wang M C; Shen H D; Lee D T; Han S H. (Department of Medical Research, Veterans General Hospital, Taipei, Taiwan, Republic of China.) ALLERGY, (1991 Oct) 46 (7) 520-8. Journal code: 39C; 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB A panel of 16 monoclonal antibodies (MoAbs) directed against Bermuda grass (Cynodon dactylon) pollen (BGP) were generated for identification and purification of the major allergenic components of the eliciting antigen (Ag). Radioimmunoprecipitation (RIP) analysis revealed that there were at least eight antigenic components with molecular weights (MW) ranging from 12 kilodalton (12 kDa) to 200 kDa. Each of these components has distinct biochemical characteristics based on sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and isoelectric focusing (IEF). Among them, Cyn d Bd67K and Cyn d Bd58K were basic proteins, Cyn d Bd35K consisted of at least four isomeric components with isoelectric points ranging from 6.2 to 7.2. The other antigens (Cyn d Bd68K, 48K, 38K, Cyn d Bd200K, Cyn d Bd46K, Cyn d Bd25K and Cyn d Bd12K) were all acidic proteins. The **IgE binding** capacity of all these antigens was determined with sera from 11 BGP-allergics by using a **modified** radioallergosorbent test. All but one of the antigens (Cyn d Bd200K) were found to react with human IgE from sera of BGP-allergic patients. Among those human **IgE-binding** molecules, Cyn d Bd35K reacted with allergic sera most frequently (10 of 11), followed by Cyn d Bd58K (8

of 11) and Cyn d Bd46K (7 of 11) respectively. Our results suggest that Cyn d Bd35K, Cyn d Bd58K, and Cyn d Bd46K are major **allergens** of BGP, and the MoAbs we obtained should be valuable tools for further purification of these **allergens**.

L19 ANSWER 42 OF 49 MEDLINE DUPLICATE 19
91206698 Document Number: 91206698. PubMed ID: 2018209. Detection of **IgE-binding** activity in serum after intranasal treatment of normal rabbits with P. judaica extract. Mistrello G; Rapisarda G; Falagiani P. (Research Department Laboratorio Farmaceutico Lofarma, Milan, Italy.) ALLERGY, (1991 Jan) 46 (1) 52-8. Journal code: 39C; 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB Local intranasal immunotherapy relieves the allergic symptoms of rhinitic patients but little is known about the absorption and distribution of inhaled **allergens** in the body. The aim of this study was to establish whether allergenic proteins are able to reach the bloodstream by penetrating through the nasal mucosa when aqueous P. judaica extract was administered into the nostrils of normal rabbits. Optimal conditions for a sensitive **modified** RAST (immunocapture RAST) were set up and the method was used to detect clinically relevant allergenic activity in the systemic circulation. The kinetic profile after intranasal treatment was compared with the profile after intravenous injection of the allergenic extract. The findings are discussed in relation to the mechanism by which local immunotherapy acts.

L19 ANSWER 43 OF 49 CAPLUS COPYRIGHT 2001 ACS
1992:589575 Document No. 117:189575 Epitopes on **allergens**. Jager, L.; Diener, C.; Mueller, W. D.; Schlenvoigt, G. (Dep. Clin. Immunol., Friedrich Schiller Univ., Jena, O-6900, Germany). New Trends Allergy III, [Int. Symp.], 3rd, Meeting Date 1990, 33-47. Editor(s): Ring, Johannes; Przybilla, Bernhard. Springer: Berlin, Germany. (English) 1991. CODEN: 58CHAG.

AB A review with 58 refs. By conventional immunol. and physicochem. techniques, natural **allergens** have been sepd. into antigenic and allergenic fractions. During the last years new methodol. developments enabled investigation of their structures in detail. The first step was the identification of antigenic and allergenic (**IgE-binding**) epitopes on these mols. This has been done for several major **allergens** from pollen, insect, fungal, and epidermal **allergens**. Usually, 2-6 antigenic and 1-3 allergenic sites have been found. In some cases, the primary structure of such epitopes or even the complete **allergen** has been uncovered. In a few of them, (Der p I, Chi t I e.g.) even the three-dimensional structure could be disclosed. Obviously sequential epitopes dominate, at least in grass pollen **allergens**. The methods which have been applied are monoclonal antibodies, improved techniques of peptide anal. and synthesis, and cloning procedures. These developments are very important both from practical and theor. points of view. They will improve diagnostic procedures and disclose th basis of often surprising cross-reactivities. More important is the fact that B-cell epitopes (being active during the manifestation of the allergic reaction) are obviously not identical with T-cell epitopes (important during sensitization). This fact could open

new ways for a scientific-based approach to immunotherapy. Other prospective developments concern the presentation of these epitopes together with MHC structures, the identification of possibly individual-specific patterns of sensitization, and a reevaluation of the exact mechanisms of the initial step of IgE-mediated reactions. The dogma that bridging of membrane-bound IgE antibodies is induced by identical epitopes obviously has to be **modified**.

L19 ANSWER 44 OF 49 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 20
91156511 EMBASE Document No.: 1991156511. The structural requirements of epitopes with **IgE binding** capacity demonstrated by three major **allergens** from fish, egg and tree pollen. Elsayed S.; Apold J.; Holen E.; Vik H.; Florvaag E.; Dybendal T.. Allergy Research Group, Lab. Clinical Biochemistry, University Hospital,N-5021 Bergen, Norway. Scandinavian Journal of Clinical and Laboratory Investigation, Supplement 51/204 (17-31) 1991.
ISSN: 0085-591X. CODEN: SCLSAH. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Three major **allergens** from cod fish, egg white and tree pollen, were characterized by studies on their allergenic and antigenic structures. The major **allergen** of cod fish, **Allergen** M 'parvalbumins pI 4.75', is composed of 113 amino acid residues with a molecular weight of 12,328 daltons. It comprised three domains, AB, CD and EF, consisting of 3 helices interspaced by one loop. Each of the loops of the CD and EF domains each coordinates one Ca2+. The antigenicity and allergenicity of **Allergen** M was deduced from studying the **modified** protein and some particular synthetic peptides. Three sites were encompassing **IgE binding** epitopes namely peptides 33-44, 65-74 and 88-96. A novel peptide (49-64), of the CD-domain, was demonstrated to be allergenically/antigenically active and cross reactive with birch pollen **allergen**, which incidentally was used as a negative control. This site encompassed two repetitive sequences (D-E-D-K) and (D-E-L-K), suggested to be mutually critical for the specificity of antibody binding. This hypothesis was reconfirmed by SPPS of several analogous peptides of region 39-64. Furthermore, peptide 88-103 of the EF-domain was similarly synthesized; it functioned as a monovalent hapten, blocking and not eliciting allergic reaction. Moreover, peptide 13-32 of domain AB, the non-calcium binding domain, was thoroughly tested. The results of PK inhibition showed clear activity and the peptide was found to function at the level of a divalent determinant. Ovalbumin (OA) is the most dominant of five major **allergens** of egg white and universally used as model protein. OA allergenic epitopes were shown to be mainly determined by the primary structure and depend on certain peptide chain length. The N-terminal decapeptide (OA-1-10) was shown to react with reaginic IgE. Direct skin test on egg allergic patients, showed no activity and the site was therefore concluded to encompass one single Ig binding haptenic epitope. Peptide OA 323-339, was demonstrated to be valuable in studies of T-cell recognition of protein antigens. Three analogous peptides of this region were prepared and clearly shown to be immunogenic in rabbits and to bind specific IgE from patients allergic to egg. OA 323-339 was concluded to encompass an allergenic and antigenic

epitope which was recognized by human and rabbit B-lymphocytes. Eight peptides in this region 11-122 were similarly synthetized. A test battery was performed to study this region using rabbit polyclonal antibodies and human specific IgE. Some of these sites were involved in binding of particular Ig paratopes. Five immunogenic peptides from the major **allergens** of tree pollen extracts (segment 23-38), were synthesized. The selection of those peptides was settled using two algorithms for providing the optimal hydrophobicity. All the synthetic peptides and analogues from region 23-38, could inhibit the binding of specific IgE to the intact molecules. A minimal requirement of an allergenic epitope was clearly demonstrated to be the repetitive four amino acid peptides interspaced by 6 unrelated spacer arm. A certain minimal molecular size of 12-15 amino acids seemed necessary in all the epitopes synthesized for studying the biological activity and for a successful predictive algorithms of the helicity.

L19 ANSWER 45 OF 49 MEDLINE

91252774 Document Number: 91252774. PubMed ID: 1710368. The structural requirements of epitopes with **IgE binding** capacity demonstrated by three major **allergens** from fish, egg and tree pollen. Elsayed S; Apold J; Holen E; Vik H; Florvaag E; Dybendal T. (Laboratory of Clinical Biochemistry, University Hospital, University of Bergen, Norway.) SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION. SUPPLEMENT, (1991) 204 17-31. Ref: 65. Journal code: UCR; 2984789R. ISSN: 0085-591X. Pub. country: Norway. Language: English.

AB Three major **allergens** from cod fish, egg white and tree pollen, were characterized by studies on their allergenic and antigenic structures. The major **allergen** of cod fish, **Allergen** M "parvalbumins pI 4.75", is composed of 113 amino acid residues with a molecular weight of 12,328 daltons. It comprised three domains, AB, CD and EF, consisting of 3 helices interspaced by one loop. Each of the loops of the CD and EF domains each coordinates one Ca2+. The antigenicity and allergenicity of **Allergen** M was deduced from studying the **modified** protein and some particular synthetic peptides. Three sites were encompassing **IgE binding** epitopes namely peptides 33-44, 65-74 and 88-96. A novel peptide (49-64), of the CD-domain, was demonstrated to be allergenically/antigenically active and cross reactive with birch pollen **allergen**, which incidentally was used as a negative control. This site encompassed two repetitive sequences (D-E-D-K) and (D-E-L-K), suggested to be mutually critical for the specificity of antibody binding. This hypothesis was reconfirmed by SPPS of several analogous peptides of region 39-64. Furthermore, peptide 88-103 of the EF-domain was similarly synthesized; it functioned as a monovalent hapten, blocking and not eliciting allergic reaction. Moreover, peptide 13-32 of domain AB, the non-calcium binding domain, was thoroughly tested. The results of PK inhibition showed clear activity and the peptide was found to function at the level of a divalent determinant. Ovalbumin (OA) is the most dominant of five major **allergens** of egg white and universally used as model protein. OA allergenic epitopes were shown to be mainly determined by the primary structure and depend on certain peptide chain length. The N-terminal decapeptide (OA 1-10) was shown to react with reaginic IgE. Direct skin test on egg allergic patients, showed no activity and the site was therefore concluded to encompasses one single

Ig binding haptenic epitope. Peptide OA 323-339, was demonstrated to be valuable in studies of T-cell recognition of protein antigens. Three analogous peptides of this region were prepared and clearly shown to be immunogenic in rabbits and to bind specific IgE from patients allergic to egg. OA 323-339 was concluded to encompass an allergenic and antigenic epitope which was recognized by human and rabbit B-lymphocytes. Eight peptides in the region 11-122 were similarly synthesized. A test battery was performed to study this region using rabbit polyclonal antibodies and human specific IgE. Some of these sites were involved in binding of particular Ig paratopes. Five immunogenic peptides from the major **allergens** of tree pollen extracts (segment 23-38), were synthesized. The selection of those peptides was setteled using two algorithms for providing the optimal hydrophobicity.(ABSTRACT TRUNCATED AT
400 WORDS)

L19 ANSWER 46 OF 49 SCISEARCH COPYRIGHT 2001 ISI (R)
91:431903 The Genuine Article (R) Number: FY740. IMMUNODETECTION METHODS FOR GRASS-POLLEN **ALLERGENS** ON WESTERN BLOTS. ONG E K; SUPHIOGLU C; SINGH M B; KNOX R B (Reprint). UNIV MELBOURNE, SCH BOT, PARKVILLE, VIC 3052, AUSTRALIA. INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY
(1990) Vol. 93, No. 4, pp. 338-343. Pub. country: AUSTRALIA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A comparison is made of eight different methods to detect allergenic proteins in Western blots of rye-grass pollen extracts. Horseradish peroxidase-based enhanced chemiluminescence (ECL) provides a sensitive method for the detection of allergenic proteins. The method has been **modified** to use more dilute solutions of ECL substrate to reduce the background, can be applied to a standard nitrocellulose membrane, and used with Kodak X-ray film. The assays can be performed rapidly, replacing
use of radiolabelled probes. Increased resolution is obtained. This makes the method suitable for detection of cDNA clones on plaque lifts, and for rapid and specific purification of proteins following immunodetection on nitrocellulose membranes.

L19 ANSWER 47 OF 49 MEDLINE DUPLICATE 21
90205876 Document Number: 90205876. PubMed ID: 1690853. Epitope mapping of the major **allergen** from yellow mustard seeds, Sin a I. Menendez-Arias L; Dominguez J; Moneo I; Rodriguez R. (Departamento de Bioquimica y Biologia Molecular I, Facultad de Ciencias, Universidad Complutense, Madrid, Spain.) MOLECULAR IMMUNOLOGY, (1990 Feb) 27 (2) 143-50. Journal code: NG1; 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The antigenic sites on the major **allergen** from yellow mustard (Sinapis alba L.) seeds were studied using murine (BALB/c) monoclonal antibodies (mAb) and human IgE antibodies. Ten IgG1 (K) mAb from two fusions were analyzed. Competition and complementation studies performed with peroxidase labeled mAb reveal the existence of two main antigenic sites in Sin a I. All the described mAb failed to recognize the unordered carboxyamidomethylated polypeptide chains, with the single exception of 2B3, which binds the alkylated large chain. However, this mAB cannot react
with the tetranitromethane-**modified** protein which retains the native conformation. This fact suggests that the only tyrosine of Sin a I,

located in the large chain, may be part of a sequential epitope of the **allergen**. This chemical modification also alters the binding of the mAb 4A11 and 3F3 to the **allergen**, besides 2B3. The three mAb belong to the same complementation group. Specific **IgE binding** cannot be inhibited either by the large or small carboxyamidomethylated polypeptide chains, while the nitrated **allergen** shows a weaker inhibitory activity than the native Sin a I. 4A11, which is a tyrosine-dependent mAb, causes the greatest binding inhibition of the tested mAb on human IgE from atopic individuals, as determined from a reverse enzyme immunoassay, suggesting an important role played by tyrosine in the immunochemical recognition of Sin a I.

L19 ANSWER 48 OF 49 MEDLINE

87286808 Document Number: 87286808. PubMed ID: 3475557. Insoluble and soluble **allergens** from wheat grain and wheat dust: detection of **IgE binding** in inhalant and ingestion allergy. Walsh B J; Baldo B A; Bass D J; Clancy R; Musk A W; Wrigley C W. NEW ENGLAND AND REGIONAL ALLERGY PROCEEDINGS, (1987 Jan-Feb) 8 (1) 27-33. Journal code: NER; 8306562. ISSN: 0742-2814. Pub. country: United States. Language: English.

AB The need for better in vitro testing for wheat allergy particularly involved correlating clinical evidence of Type I hypersensitivity with laboratory detection of specific IgE antibodies in serum. We report here an improvement in this relationship by the use of a **modified** method for RAST (Radioallergosorbent test), involving nitrocellulose as the solid phase and alkali (or ethanol) for extraction of **allergens** and treatment of discs. Serum IgE reactions with the full range of wheat grain and dust proteins were studied using this method and the results were related to wheat allergies due to flour ingestion and the inhalation of flour, pollen or grain dust.

L19 ANSWER 49 OF 49 MEDLINE DUPLICATE 22

85235315 Document Number: 85235315. PubMed ID: 3839248. A comparison of the binding of IgE in the sera of patients with bakers' asthma to soluble and insoluble wheat-grain proteins. Walsh B J; Wrigley C W; Musk A W; Baldo B A. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1985 Jul) 76 (1) 23-8. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB The **IgE-binding** proteins from flour, associated with bakers' asthma, have been reassessed by use of a **modified** RAST suitable for both soluble and insoluble proteins. Nitrocellulose sheet was used for preparing RAST discs, and seven different solvents were compared for their suitability in preparing discs. Dilute alkali (1% potassium hydroxide) was chosen as the best solvent for disc preparation, and its use was compared with that of water as solvent. RAST analyses of sera from 24 allergic bakers demonstrated that the albumin fraction of flour is clearly allergenic (as found in previous studies), but in addition, major **IgE-binding** proteins were found in the other three fractions (globulin, gliadin, and glutenin) when potassium hydroxide was the solvent (but not with water). We conclude that current RAST procedures, which favor water-soluble **allergens**, are inadequate because they do not satisfactorily test for water-insoluble **allergens**.

=> s (bannon g?/au or burks w?/au or sampson h?/au or sosin h?/au)

L20 1793 (BANNON G?/AU OR BURKS W?/AU OR SAMPSON H?/AU OR SOSIN H?/AU)

=> s l20 and allergen

L21 399 L20 AND ALLERGEN

=> s l21 and peanut

L22 221 L21 AND PEANUT

=> dup remove l22

PROCESSING COMPLETED FOR L22
L23 114 DUP REMOVE L22 (107 DUPLICATES REMOVED)

=> s l23 and IgE

L24 71 L23 AND IGE

=> s l24 and amino acid substitution

L25 3 L24 AND AMINO ACID SUBSTITUTION

=> dup remove l25

PROCESSING COMPLETED FOR L25
L26 3 DUP REMOVE L25 (0 DUPLICATES REMOVED)

=> d l26 1-3 cbib abs

L26 ANSWER 1 OF 3 MEDLINE
2000148681 Document Number: 20148681. PubMed ID: 10669862. Mutational analysis of the **IgE**-binding epitopes of P34/Gly m Bd 30K. Helm R M; Cockrell G; Connaughton C; West C M; Herman E; **Sampson H A**; **Bannon G A**; Burks A W. (Department of Pediatrics, University of Arkansas for Medical Sciences, Arkansas Children's Nutrition Center, Little Rock, AR 72202, USA.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (2000 Feb) 105 (2 Pt 1) 378-84. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: **Peanuts** and soybeans are 2 foods that have been shown to be responsible for many atopic disorders. Because of their nutritional benefit, soybean proteins are now being used increasingly in a number of food products. Previous studies have documented multiple **allergens** in soybean extracts, including glycinin, beta-conglycinin, and the P34/Gly m Bd 30K protein. OBJECTIVE: Our overall goal was to identify soybean-specific **allergens** to begin to understand molecular and immunochemical characteristics of legume proteins. The specific aim of the current investigation was to identify the essential amino acid residues necessary for **IgE** binding in the 5 distinct immunodominant epitopes of P34/Gly m Bd 30K. METHODS: Serum

IgE from 6 clinically sensitive soybean-allergic individuals was used to identify P34/Gly m Bd 30K in the native and single amino acid substituted peptides with use of the SPOTS peptide synthesis technique to determine critical amino acids required for **IgE** binding. RESULTS: The intensity of **IgE** binding and epitope recognition by serum **IgE** from the individuals varied substantially. With use of serum from 6 clinically soybean-sensitive individuals, 2 of the 5 immunodominant epitopes could be mutagenized to non-**IgE** binding peptides. CONCLUSIONS: Single-site **amino acid substitution** of the 5 immunodominant epitopes of Gly m Bd 30K with alanine revealed that **IgE** binding could be reduced or eliminated in epitopes 6 and 16 in the serum obtained from 6 soybean-sensitive patients.

L26 ANSWER 2 OF 3 MEDLINE

2001086248 Document Number: 20564013. PubMed ID: 11112857. A soybean G2 glycinin **allergen**. 2. Epitope mapping and three-dimensional modeling. Helm R M; Cockrell G; Connaughton C; **Sampson H A**; **Bannon G A**; Beilinson V; Nielsen N C; Burks A W. (Department of Pediatrics, University of Arkansas for Medical Sciences, Arkansas Children's Nutrition Center, Little Rock, AR 72202-3591, USA.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2000 Nov) 123 (3) 213-9. Journal code: BJ7. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Multiple **allergens** have been documented in soybean extracts. **IgE** from individuals allergic to soybeans, but not to **peanut**, has been shown by immunoblot analysis to bind to proteins with a molecular weight of approximately 22 kD. These findings suggested that this unique protein fraction from soybean might be responsible, in part, for soybean allergic reactivity. The objective of the present study was to characterize specific B cell epitopes, to determine if any amino acid was critical to **IgE** binding and to model the 22-kD G2 soybean **allergen** to the three-dimensional (3-D) phaseolin molecule. METHODS: B cell epitopes were identified using SPOTs peptide analysis. Structural orientation of the **IgE**-binding regions was mapped to the 3-D phaseolin molecule using molecular modeling of the protein tertiary structure. RESULTS: Eleven linear epitopes, representing 15 amino acid peptide sequences, bound to **IgE** in the glycinin molecule. These epitopes were predicted to be distributed asymmetrically on the surface of G2 trimers. CONCLUSIONS: Only 1 epitope could be rendered non-**IgE** binding by alanine substitutions in the peptide. The nonrandom distribution of the **IgE** binding sites provides new insight into their organization in trimers in 11S complexes of the G2 glycinin **allergen**.

L26 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS

1999:594994 Document No. 131:227660 Tertiary structure of **peanut allergen** Ara h 1. **Burks, Wesley, Jr.**; Helm, Ricki M.; Cockrell, Gael; **Bannon, Gary A.**; Stanley, J. Steven; Shin, David S.; **Sampson, Hugh**; Compadre, Cesar M.; Huang, Shau K. (Board of Trustees of the University of Arkansas, USA). PCT Int. Appl. WO 9945961 A1 19990916, 193 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH,

CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US5494 19990312. PRIORITY: US 1998-PV77763 19980312.

AB Ara h 1, a major **peanut allergen**, has been isolated and shown to contain 23 linear **IgE**-binding epitopes, 6-10 residues in length. Anal. of wild-type and mutant peptides with single **amino acids substitutions** showed that amino acids residing in the middle of the epitope were more crit. for **IgE** binding; that polar charged residues occurred more frequently within the epitope while apolar residues were more important for **IgE** binding; and that a single **amino acid substitution** in an epitope resulted in a loss of ability to bind **IgE**. In addn., a homol.-based mol. model of the Ara h 1 protein representing residues 171-586 was made and allowed visualization of epitopes 10-22. The majority of these epitopes appear clustered and many of the crit. amino acids involved in binding are evenly distributed on the surface. The information from the mutational anal. and the mol. model will aid in the design of immunotherapies.

=> d his

(FILE 'HOME' ENTERED AT 18:31:19 ON 05 JUN 2001)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 18:31:32 ON 05 JUN 2001

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L1         91377 S ALLERGEN
L2          2043 S L1 AND MODIFIED
L3           804 S L2 AND IGE
L4           114 S L3 AND IGE BINDING
L5             3 S L4 AND IGG BINDING
L6             3 DUP REMOVE L5 (0 DUPLICATES REMOVED)
L7             1 S L4 AND AMINO ACID SUBSTITUTION
L8           105 S L3 AND AMINO ACID
L9             7 S L3 AND AMINO ACID SUBSTITUTION
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FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 18:36:53 ON 05 JUN 2001

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L10        91377 S ALLERGEN
L11         2043 S L10 AND MODIFIED
L12            7 S L11 AND AMINO ACID SUBSTITUTION
L13            4 DUP REMOVE L12 (3 DUPLICATES REMOVED)
L14            0 S L11 AND AMINO ACID DELETION
L15            0 S L11 AND AMINO ACID ADDITION
L16          114 S L11 AND IGE BINDING
L17            4 S L16 AND DECREASE
L18            2 DUP REMOVE L17 (2 DUPLICATES REMOVED)
L19           49 DUP REMOVE L16 (65 DUPLICATES REMOVED)
L20         1793 S (BANNON G?/AU OR BURKS W?/AU OR SAMPSON H?/AU OR SOSIN H?/AU)
L21          399 S L20 AND ALLERGEN
L22          221 S L21 AND PEANUT
L23          114 DUP REMOVE L22 (107 DUPLICATES REMOVED)
L24           71 S L23 AND IGE
L25            3 S L24 AND AMINO ACID SUBSTITUTION
L26            3 DUP REMOVE L25 (0 DUPLICATES REMOVED)
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=> s l21 and legumes

L27 15 L21 AND LEGUMES

=> dup remove l27

PROCESSING COMPLETED FOR L27
L28 9 DUP REMOVE L27 (6 DUPLICATES REMOVED)

=> d l28 1-9 cbib abs

L28 ANSWER 1 OF 9 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
1998274352 EMBASE Peanut **allergens**. **Burks W.**;
Sampson H.A.; **Bannon G.A.**. Dr. W. Burks, Department of Pediatrics, Div. of Pediatric Allergy/Immunol., 800 Marshall Street, Little Rock, AR 72207, United States. Allergy: European Journal of Allergy and Clinical Immunology 53/8 (725-730) 1998.
Refs: 33.
ISSN: 0105-4538. CODEN: LLRGDY. Pub. Country: Denmark. Language: English.
Summary Language: English.
AB The development of an IgE response to an **allergen** involves a series of interactions between T cells and B cells. B cells bearing appropriate antigen-specific surface immunoglobulins interact with proliferating **allergen**-specific T cells, leading to isotype switching and the generation of antigen-specific IgE. The antigen-specific IgE then binds to the Fc(.epsilon.)RI receptors of mast cells and basophils. Because antigen-specific IgE plays such a critical role in the pathogenesis of allergic disease, determination of **allergen**-specific, IgE-binding epitopes is an important first step toward a better understanding of this complex disease process. Studies defining the peanut **allergens** should now allow more specific research to be done on improved diagnostic methods for peanut hypersensitivity, new immunotherapeutic approaches for this chronic and often severe disease, and development of hypoallergenic or less sensitizing plants. Immediate hypersensivity reactions to foods are mediated through the interaction of IgE with a specific food protein. While specific IgE-binding epitopes from the major **allergens** of cow's milk (25), codfish (26), hazelnut (27), soybeans (28), and shrimp (29) have been elucidated, there have been few, if any, common characteristics found in these binding sites. Our work on the IgE- binding sites of Ara h 1, 2, and 3 indicates that there are no common amino- acid sequence motifs shared by these epitopes. However, we have determined that in the IgE-binding epitopes of these **allergens** the hydrophobic amino- acid residues appear to play a critical role in IgE binding. The observation that alteration of a single amino acid leads to the loss of IgE binding in a population of peanut-sensitive individuals is significant because it suggests that while each patient may display a polyclonal IgE reaction to a particular

allergen (16, 17), IgE from different patients recognize the same epitope and must interact with that epitope in a similar fashion. Besides after the finding that many epitopes in each of the different peanut **allergens** contained more than one residue critical for IgE binding, it was also determined that more than on residue type (ala or met) could be substituted at certain positions in an epitope with similar results. This information may allow the design of a hypoallergenic protein that would be effective in blunting allergic reactions for a population of peanut-sensitive individuals. Furthermore, a peanut from which the IgE-binding epitopes of the major **allergens** have been removed may prevent the development of peanut hypersensitivity in individuals genetically predisposed. The characteristics that have been attributed to allergenic proteins include their abundance in the food source, their resistance to food processing, and their stability to digestion by the gastrointestinal tract (30-32). The major **allergens** of foods - in particular, the Ara h 1 peanut **allergen** - have been shown to survive intact most food-processing methods and to be stable to digestion in in vitro systems designed to mimic the gastrointestinal tract. Our observations on the tertiary structure of the Ara h 1 monomer and the determination that this protein readily forms a trimeric complex may help to determine why this protein is allergenic. While there are numerous protease digestion sites throughout the length of this protein, the structure may be so compact that potential cleavage sites are inaccessible until the protein is denatured. The physical properties of the Ara h 1 molecule and the other peanut **allergens** may help to explain the extreme allergenicity exhibited by peanut proteins. The only therapeutic option currently available for the prevention of a peanut hypersensitivity reaction is food avoidance. Unfortunately, for a ubiquitous food such as peanut, the possibility of an inadvertent ingestion is great. Interestingly, most of the peanut **allergens** identified to date, including Ara h 1, 2, and 3, have sequence homology with proteins in other plants. This information may help to begin to explain the cross-reacting IgE antibodies to other **legumes** that are found in the sera of patients that manifest clinical symptoms to only one member of the legume family (33). Certainly, the elucidation of the position of the Ara h 1-binding epitopes clustered on the surface of the molecule may enable us to understand why these regions elicit the clinical symptoms associated with peanut hypersensitivity. Perhaps the presentation of multiple, clustered epitopes to mast cells results in a more efficient and dramatic release of mediators, resulting, in turn, in the more severe clinical symptoms observed in patients with peanut hypersensitivity. Current work is exploring this possibility by comparing the IgE-binding epitopes and tertiary structures of other legume **allergens**. Taken in total, these studies suggest that an altered Ara h 1, 2, or 3 gene could be developed to replace its allergenic homologue in the peanut genome, thus blunting allergic reactions in sensitive individuals who inadvertently ingest this food. Since these gene products are an abundant and integral seed storage protein, it would be necessary for the altered protein to retain as much of its native function, properties, and three-dimensional structure as possible. The information gained from these studies on the peanut **allergens** indicates that development of hypoallergenic seed storage proteins may be feasible. Additionally, a less allergenic peanut protein with the immunodominant IgE epitopes mutated, rather than

the current peanut protein as we know it, may prove to be beneficial in feeding the at-risk group of atopic individuals. However, the effect that altering critical amino acids within each of the IgE-binding epitopes has on the properties of the seed storage proteins is currently unknown. In view of the widespread use of peanuts in consumer foods and the potential risk this poses to individuals genetically predisposed to developing peanut allergy and to the health of individuals already peanut sensitive, this approach is currently being explored in our laboratories.

L28 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2001 ACS
1998:141656 Characterization and epitope analysis of ARA h 3, a glycinin involved in peanut hypersensitivity.. Helm, Erica M.; Rabjohn, Pat A.; Stanley, J. Steven; West, C. Michael; Huang, S. K.; **Sampson, H.**; Burks, A. Wesley; **Bannon, Gary A.** (Department Chemistry, Hendrix College, Conway, AR, 72032, USA). Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2, CHED-179. American Chemical Society: Washington, D. C. (English) 1998. CODEN: 65QTAA.
AB Peanut allergy is a major health concern due to the severity of the allergic reaction, the lifelong persistence of the allergy, and the ubiquitous use of peanut as a protein supplement in processed foods. Using a previously unidentified peanut **allergen**, Ara h 3 cDNA clone was isolated, sequenced and found to be 1530 nucleotides and encoded a 510 amino acid protein. This sequence showed homol. to the glycinin family of seed storage proteins of common **legumes**. Synthetic peptides were used to det. which regions of the primary sequence served as linear B-cell epitopes for binding serum IgE from a population of peanut hypersensitivity patients. These epitopes were distributed evenly throughout the primary sequence and were six to ten amino acids in length. Further studies will be focused on identifying individual amino acids crit. for IgE binding. Once these amino acids are identified, it will be possible to mutate crit. residues to eliminate the ability of this protein to bind IgE.

L28 ANSWER 3 OF 9 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
1998398562 EMBASE **Legumes**, eggs, and milk. **Sampson H.A.**.
Dr. H.A. Sampson, Department of Pediatrics, Box 1198, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029-6547, United States. Allergy: European Journal of Allergy and Clinical Immunology, Supplement 53/46 (38-43) 1998.
Refs: 60.
ISSN: 0108-1675. CODEN: ALSUET. Pub. Country: Denmark. Language: English.

L28 ANSWER 4 OF 9 SCISEARCH COPYRIGHT 2001 ISI (R)
1998:789006 The Genuine Article (R) Number: 126KQ. Cellular and molecular characterization of a major soybean **allergen**. Helm R M (Reprint); Cockrell G; Herman E; Burks A W; **Sampson H A**; **Bannon G A**. UNIV ARKANSAS MED SCI, RES INST, DEPT PEDIAT, ARKANSAS CHILDRENS HOSP, 1120 MARSHALL ST, LITTLE ROCK, AR 72202 (Reprint); UNIV ARKANSAS MED SCI, RES INST, DEPT BIOCHEM & MOL BIOL, ARKANSAS CHILDRENS HOSP, LITTLE ROCK, AR 72202; AGR RES SERV, USDA, BELTSVILLE, MD; MT SINAI SCH MED, DIV PEDIAT ALLERGY & IMMUNOL, NEW YORK, NY. INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (SEP 1998) Vol. 117, No. 1, pp. 29-37.

Publisher: KARGER. ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
ISSN: 1018-2438. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Soybean proteins share a large number of cross-reacting **allergens** with other members of the legume family; however, soy-allergic patients rarely react clinically to other members of the legume family. Gly m Ed 30K, an IgE-binding protein with a molecular weight of 30 kD, was identified in soybean extracts by Western IgE-immunoblot analysis. This monomeric **allergen** was shown to have an N-terminal amino acid sequence and amino acid composition identical to that of the seed 34-kD protein, P34, a thiol protease of the papain family, Electronmicroscopic immunolocalization of P34 monoclonal antibodies and IgE binding to sections of soybean seeds showed dense staining throughout the vacuolar bodies, localizing the **allergens** in protein storage vacuoles of seed cotyledons. We used pooled serum from soybean-sensitive patients to determine the linear IgE-specific epitopes in the 34-kD **allergen** amino acid sequence. B-cell epitope mapping revealed 10 regions of IgE-binding activity using an overlapping peptide strategy of 15-mers offset by 8 amino acids throughout the P34 sequence. Smaller overlapping peptides, 10-mers offset by 2 amino acids, revealed 16 distinct linear epitopes, 9 of which were mapped to the mature protein. No obvious amino acid sequence motifs could be identified by the smaller IgE-binding epitopes. Using individual patient serum, 5 immunodominant epitopes were identified in this **allergen**.

L28 ANSWER 5 OF 9 MEDLINE DUPLICATE 2
97093624 Document Number: 97093624. PubMed ID: 8939161. Identification of unique peanut and soy **allergens** in sera adsorbed with cross-reacting antibodies. Eigenmann P A; Burks A W; **Bannon G A; Sampson H A.** (Johns Hopkins University School of Medicine, Baltimore, MD, USA.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1996 Nov) 98 (5 Pt 1) 969-78. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Soybean and peanut are members of the legume family and share several common antigenic fractions. Patients allergic to one of these foods have serum IgE antibodies that immunologically cross-react with other **legumes**. Nevertheless, ingestion of other **legumes** generally does not induce an allergic reaction, suggesting that cross-reacting antibodies are not clinically relevant. OBJECTIVE: This study was designed to identify unique peanut or soybean antigenic fractions, with sera adsorbed to remove cross-reacting antibodies, thus resulting in sera with IgE antibodies unique to either soy or peanut. METHODS: Cross-reacting antibodies to soy were removed from the sera of two patients allergic to peanut and soy and three patients allergic to peanut by soy-affinity chromatography. Cross-reacting antibodies to peanut were adsorbed from the sera of a patient allergic to peanut and soy and a patient allergic to peanut by peanut-affinity chromatography. Adequate removal of cross-reacting antibodies was verified by ELISA after each adsorption step. Unadsorbed sera and sera adsorbed to remove cross-reacting antibodies (either to soy or to peanut) were assayed for specific IgE binding to peanut or soy immunoblots. RESULTS: Unique peanut-specific IgE antibodies (i.e., soy antibody-adsorbed) were found to bind to peanut fractions at 46, 29, 25, 19, 17, 14, and 5 kd on immunoblots of whole peanut protein. Similarly, unique soy-specific IgE

(i.e., peanut antibody-adsorbed) were found to bind a fraction at 46 kd, and to a lesser extent, to a fraction at 21 kd on immunoblots of whole soy protein. The 73% reduction of IgE antibody binding to peanut by ELISA after adsorption of cross-reacting antibodies indicates extensive cross-reactivity between soy and peanut antigens. CONCLUSIONS: Antigen-affinity chromatography is an effective method for removal of cross-reacting antibodies. We identified IgE antibody binding (with sera where cross-reacting antibodies were removed) to several unique antigenic fractions of peanut and soy. Further studies will determine the clinical significance of these fractions in IgE-mediated food hypersensitivity reactions.

L28 ANSWER 6 OF 9 SCISEARCH COPYRIGHT 2001 ISI (R)
95:707219 The Genuine Article (R) Number: RY954. RECOMBINANT PEANUT **ALLERGEN** ARA-H-I EXPRESSION AND IGE BINDING IN PATIENTS WITH PEANUT HYPERSENSITIVITY. BURKS A W (Reprint); COCKRELL G; STANLEY J S; HELM R M; **BANNON G A**. ARKANSAS CHILDRENS HOSP, 800 MARSHALL ST, LITTLE ROCK, AR, 72202 (Reprint); UNIV ARKANSAS MED SCI HOSP, DEPT PEDIAT, LITTLE ROCK, AR, 72205; UNIV ARKANSAS MED SCI HOSP, DEPT BIOCHEM & MOLEC BIOL, LITTLE ROCK, AR, 72205. JOURNAL OF CLINICAL INVESTIGATION (OCT 1995)
Vol. 96, No. 4, pp. 1715-1721. ISSN: 0021-9738. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Peanut allergy is a significant health problem because of the frequency, the potential severity, and the chronicity of the allergic sensitivity. Serum IgE from patients with documented peanut hypersensitivity reactions and a peanut cDNA expression library were used to identify clones that encode peanut **allergens**. One of the major peanut **allergens**, Ara h I, was selected from these clones using Ara h I specific oligonucleotides and polymerase chain reaction technology. The Ara h I clone identified a 2.3-kb mRNA species on a Northern blot containing peanut poly (A)(+) RNA. DNA sequence analysis of the cloned inserts revealed that the Ara h I **allergen** has significant homology with the vicilin seed storage protein family found in most higher plants, The isolation of the Ara h I clones allowed the synthesis of this protein in E. coli cells and subsequent recognition of this recombinant protein in immunoblot analysis using serum IgE from patients with peanut hypersensitivity. With the production of the recombinant peanut protein it will now be possible to address the pathophysiologic and immunologic mechanisms regarding peanut hypersensitivity reactions specifically and food hypersensitivity in general.

L28 ANSWER 7 OF 9 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
90008800 EMBASE Document No.: 1990008800. Cross-allergenicity in the legume botanical family in children with food hypersensitivity. II. Laboratory correlates. Bernhisel-Broadbent J.; Taylor S.; **Sampson H.A.**. Johns Hopkins Hospital, CMSC-1103, 600 N. Wolfe St.,Baltimore, MD 21205, United States. Journal of Allergy and Clinical Immunology 84/5 I (701-709) 1989.
ISSN: 0091-6749. CODEN: JACIBY. Pub. Country: United States. Language: English. Summary Language: English.
AB Only two of 41 legume-allergic patients diagnosed by double-blind, placebo-controlled oral food challenge or 'convincing history' of

anaphylaxis had an IgE-mediated hypersensitivity reaction to more than one
member of the legume family. However, extensive immunologic cross-reactivity was demonstrated among legume antigens on Immunoblot and Immunodot-blot analyses and prick skin tests. The proteins of six **legumes** (peanut, soybean, lima bean, pea, garbanzo bean, and gree beans) were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, transferred to nitrocellulose, and probed with sera from six legume-allergic patients. Multiple IgE-binding bands were identified in each legume lane by the sera from each of these legume-allergic patients. In vitro cross-reactivity did not correlate with clinical hypersensitivity. All the **legumes** studied (except green bean) had a prominent band at 20 kd. Numerous proteins and protein subunits can be identified in each of the **legumes** (16 peanut, 21 soybean, 23 lima bean, 25 pea, 22 garbanzo bean, and 11 green bean protein bands) by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, and it appears that legume-allergic patients' sera may recognize multiple similar fractions from each legume. A second in vitro test was performed in which the six legume extracts were bound directly onto nitrocellulose paper. These 'legume' Immunodot blots were probed for specific IgE-binding activity with sera from 62 patients with positive legume prick skin tests.
The legume Immunodot blots again demonstrated extensive clinically irrelevant cross-reactivity. However, this test may prove useful as a simple technique for screening food-specific IgE with minimal quantities of sera.

L28 ANSWER 8 OF 9 MEDLINE DUPLICATE 3
89140114 Document Number: 89140114. PubMed ID: 2918186.
Cross-allergenicity in the legume botanical family in children with food hypersensitivity. Bernhisel-Broadbent J; **Sampson H A.**
(Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD 21205.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1989 Feb) 83 (2 Pt 1) 435-40. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB Sixty-nine patients with one or more positive prick skin tests to **legumes** (peanut, soybean, green bean, pea, and lima bean) were evaluated for food hypersensitivity with in-hospital oral food challenges.
Of the 280 prick skin tests to **legumes** performed, 130 were positive. Forty-three positive food challenges occurred in 41 patients. The prevalence of legume allergy was not statistically different in those patients (N = 36) with two or more positive legume prick skin test (64% positive) compared to those patients (N = 33) with only one positive legume prick skin test (55% positive; p greater than 0.10). Even in this selected patient population, only two patients had symptomatic hypersensitivity to two **legumes**. Among patients with a positive prick skin test to peanut (N = 60), the mean wheal size was larger in patients with a positive versus a negative oral food challenge to peanut (p less than 0.001). Results of oral food challenges demonstrate that clinically important cross-reactivity to **legumes** in children is very rare. Clinical hypersensitivity to one legume does not warrant dietary elimination of all **legumes**. Results of prick skin tests should not be used to determine prolonged food restriction diets.

L28 ANSWER 9 OF 9 MEDLINE
88299445 Document Number: 88299445. PubMed ID: 3403872. Allergenic cross-reactivity among legume foods. Bock S A; Atkins F M; **Sampson H**

A. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1988 Aug) 82 (2) 310-2. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

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(FILE 'HOME' ENTERED AT 18:31:19 ON 05 JUN 2001)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 18:31:32 ON 05 JUN 2001

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L1         91377 S ALLERGEN
L2          2043 S L1 AND MODIFIED
L3           804 S L2 AND IGE
L4           114 S L3 AND IGE BINDING
L5             3 S L4 AND IGG BINDING
L6             3 DUP REMOVE L5 (0 DUPLICATES REMOVED)
L7             1 S L4 AND AMINO ACID SUBSTITUTION
L8           105 S L3 AND AMINO ACID
L9             7 S L3 AND AMINO ACID SUBSTITUTION
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FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 18:36:53 ON 05 JUN 2001

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L10        91377 S ALLERGEN
L11         2043 S L10 AND MODIFIED
L12            7 S L11 AND AMINO ACID SUBSTITUTION
L13            4 DUP REMOVE L12 (3 DUPLICATES REMOVED)
L14            0 S L11 AND AMINO ACID DELETION
L15            0 S L11 AND AMINO ACID ADDITION
L16          114 S L11 AND IGE BINDING
L17            4 S L16 AND DECREASE
L18            2 DUP REMOVE L17 (2 DUPLICATES REMOVED)
L19           49 DUP REMOVE L16 (65 DUPLICATES REMOVED)
L20         1793 S (BANNON G?/AU OR BURKS W?/AU OR SAMPSON H?/AU OR SOSIN
H?/AU)
L21          399 S L20 AND ALLERGEN
L22          221 S L21 AND PEANUT
L23          114 DUP REMOVE L22 (107 DUPLICATES REMOVED)
L24           71 S L23 AND IGE
L25            3 S L24 AND AMINO ACID SUBSTITUTION
L26            3 DUP REMOVE L25 (0 DUPLICATES REMOVED)
L27           15 S L21 AND LEGUMES
L28            9 DUP REMOVE L27 (6 DUPLICATES REMOVED)
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=> s l21 and milks

L29 0 L21 AND MILKS

=> s l21 and grains

L30 1 L21 AND GRAINS

=> d l30 cbib abs

L30 ANSWER 1 OF 1 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
95280168 EMBASE Document No.: 1995280168. Immunologic cross-reactivity among

cereal **grains** and grasses in children with food hypersensitivity. Jones S.M.; Magnolfi C.F.; Cooke S.K.; **Sampson H.A.**. Johns Hopkins Hospital, CMSC 1103, 600 N. Wolfe,Baltimore, MD 21287, United States. Journal of Allergy and Clinical Immunology 96/3 (341-351) 1995.
ISSN: 0091-6749. CODEN: JACIBY. Pub. Country: United States. Language: English. Summary Language: English.

AB Background: Because of a lack of clinical data from food challenges, allergists often recommend dietary restriction of all cereal **grains** in patients with sensitivity to at least one grain. Objectives: The purposes of this study were to assess the degree of intrabotanical cross-reactivity among cereal **grains** and related grasses, to better define the prevalence of multiple grain hypersensitivity, and to define the protein fractions associated with wheat hypersensitivity. Methods: One hundred forty-five patients evaluated by food challenges and skin prick tests were divided into three groups: group 1, cereal grain and grass allergies; group 2, wheat allergy alone; and group 3, grass allergy alone. Fifteen patients were further selected from groups 1 to 3. Sodium dodecylsulfate-polyacrylamide gel electrophoresis and immunoblot analyses were performed on six **grains** and four related grasses with sera from these patients. Results: Only 21% of patients had symptomatic reactivity as determined by food challenge; 80% had reactivity to only one grain. As determined by immunoblot analyses, patients in groups 1 and 2 showed extensive cross-reactivity (within each group) among **grains** but little cross-reactivity among grasses, whereas patients in group 3 showed cross-reactivity between the **grains** and grasses. Patients with wheat allergy had specific IgE binding to wheat fractions 47 kd and 20 kd, bands not recognized by patients with grass allergy. Conclusions: Clinically insignificant cross-reactivity exists among cereal **grains** and grasses; therefore, elimination of all **grains** from the diet of a patient with grain allergy is unwarranted. Further purification and characterization of the 47 kd and 20 kd wheat fractions is needed to provide more specific in vitro testing.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 18:31:32 ON 05 JUN 2001

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L1         91377 S ALLERGEN
L2          2043 S L1 AND MODIFIED
L3           804 S L2 AND IGE
L4           114 S L3 AND IGE BINDING
L5             3 S L4 AND IGG BINDING
L6             3 DUP REMOVE L5 (0 DUPLICATES REMOVED)
L7             1 S L4 AND AMINO ACID SUBSTITUTION
L8           105 S L3 AND AMINO ACID
L9             7 S L3 AND AMINO ACID SUBSTITUTION
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FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 18:36:53 ON 05 JUN 2001

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L10        91377 S ALLERGEN
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L11        2043 S L10 AND MODIFIED
L12           7 S L11 AND AMINO ACID SUBSTITUTION
L13           4 DUP REMOVE L12 (3 DUPLICATES REMOVED)
L14           0 S L11 AND AMINO ACID DELETION
L15           0 S L11 AND AMINO ACID ADDITION
L16         114 S L11 AND IGE BINDING
L17           4 S L16 AND DECREASE
L18           2 DUP REMOVE L17 (2 DUPLICATES REMOVED)
L19          49 DUP REMOVE L16 (65 DUPLICATES REMOVED)
L20        1793 S (BANNON G?/AU OR BURKS W?/AU OR SAMPSON H?/AU OR SOSIN
H?/AU)
L21         399 S L20 AND ALLERGEN
L22         221 S L21 AND PEANUT
L23         114 DUP REMOVE L22 (107 DUPLICATES REMOVED)
L24          71 S L23 AND IGE
L25           3 S L24 AND AMINO ACID SUBSTITUTION
L26           3 DUP REMOVE L25 (0 DUPLICATES REMOVED)
L27          15 S L21 AND LEGUMES
L28           9 DUP REMOVE L27 (6 DUPLICATES REMOVED)
L29           0 S L21 AND MILKS
L30           1 S L21 AND GRAINS

=> s l21 and eggs

L31          16 L21 AND EGGS

=> dup remove l31

PROCESSING COMPLETED FOR L31
L32          11 DUP REMOVE L31 (5 DUPLICATES REMOVED)

=> d l32 1-11 cbib abs


L32  ANSWER 1 OF 11  EMBASE  COPYRIGHT 2001 ELSEVIER SCI. B.V.
1999251951  EMBASE  Anaphylaxis and food hypersensitivity. Burks A.W. Jr.;
     Jones S.M.; Wheeler J.G.; Sampson H.A.. Dr. A.W. Burks Jr.,
     Department of Pediatrics, University Arkansas Medical Sciences, Arkansas
     Children's Hospital, 1120 Marshall Street, Little Rock, AR 72202, United
     States. Immunology and Allergy Clinics of North America  19/3 (533-552)
     1999.
     Refs: 66.
     ISSN: 0889-8561. CODEN: INCAEP. Pub. Country: United States. Language:
     English. Summary Language: English.
AB   Anaphylaxis is a syndrome that has diverse causes and a diverse
     presentation of symptoms associated with type I IgE-mediated
     hypersensitivity. Anaphylaxis is recognized by cutaneous, respiratory,
     gastrointestinal, and cardiovascular signs and symptoms that occur alone
     or together. Recent studies have highlighted the prevalence of
     food-induced anaphylactic reactions, and have shown that certain foods
are
     the most common cause of anaphylaxis outside of the hospital. Foods that
     most often precipitate an anaphylactic episode in children are milk,
     eggs, and peanuts; in adults, most episodes are caused by peanuts,
     tree nuts, fish, and shellfish. An accurate diagnosis should be made in
     food-induced anaphylaxis so that the offending food allergen can
     be eliminated from the diet. New developments in the treatment of
allergic
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disease, including immunotherapy, are likely to have a significant impact in this area.

L32 ANSWER 2 OF 11 MEDLINE
2000065236 Document Number: 20065236. PubMed ID: 10597368. Biochemistry of food **allergens**. Stanley J S; **Bannon G A**.
(Department of Pediatrics and Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock 72205, USA.)
CLINICAL REVIEWS IN ALLERGY AND IMMUNOLOGY, (1999 Fall) 17 (3) 279-91.
Ref: 53. Journal code: CA0; 9504368. ISSN: 1080-0549. Pub. country: United States. Language: English.

L32 ANSWER 3 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
1998398562 EMBASE Legumes, **eggs**, and milk. **Sampson H.A.**.
Dr. H.A. Sampson, Department of Pediatrics, Box 1198, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029-6547, United States. Allergy: European Journal of Allergy and Clinical Immunology, Supplement 53/46 (38-43) 1998.
Refs: 60.
ISSN: 0108-1675. CODEN: ALSUET. Pub. Country: Denmark. Language: English.

L32 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2001 ACS
1998:529990 Egg **allergens**.. **Sampson, Hugh A.** (Mount Sinai School Medicine, New York, NY, 10029-6574, USA). Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27, AGFD-005. American Chemical Society: Washington, D. C. (English) 1998. CODEN: 66KYA2.
AB **Eggs** are one of the most common causes of food allergic reactions in children. The egg yolk proteins are considered less allergenic than those of the egg white, although IgE antibodies to chicken gamma globulin, apovitellenin I, and contaminating egg white proteins can be demonstrated. The egg white contains 23 different glycoproteins, most of which have been purified and their amino acid sequences detd. Ovomucoid (Gal d 1), ovalbumin (Gal d 2), ovotransferin (Gal d 3), and lysozyme (Gal d 4) have been identified as major **allergens**, but ovomucoid has been shown to be the dominant **allergen**. Ovomucoid comprises 10% and ovalbumin greater than 50% of the total egg white protein, and both are easily demonstrable in raw and cooked **eggs**. Both in vitro and in vivo studies have demonstrated that ovomucoid [Gal d 1] is the dominant **allergen** in hen's egg, and children with persistent egg allergy have significantly higher concns. of IgE anti-ovomucoid antibodies than those who "outgrow" their reactivity.

L32 ANSWER 5 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
1997:509530 Document No.: PREV199799808733. Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. **Sampson, Hugh A.** (1); Ho, Deborah G.. (1) Johns Hopkins Hosp., CMSC 1102, 600 N. Wolfe St., Baltimore, MD 21287-3923 USA. Journal of Allergy and Clinical Immunology, (1997) Vol. 100, No. 4, pp. 444-451. ISSN: 0091-6749. Language: English.
AB Background: The double-blind, placebo-controlled food challenge (DBPCFC) is the "gold standard" for diagnosis of food hypersensitivity. Skin prick tests and RASTs are sensitive indicators of food-specific IgE antibodies

but poor predictors of clinical reactivity. Previous studies suggested that high concentrations of food-specific IgE antibody were predictive of food-induced clinical symptoms. Because the CAP System FEIA (Pharmacia Diagnostics, Uppsala, Sweden) provides a quantitative assessment of **allergen**-specific IgE antibody, this study was undertaken to determine the potential utility of the CAP System FEIA in diagnosis of IgE-mediated food hypersensitivity- Methods: Sera from 196 patients with food allergy were analyzed for specific IgE antibodies to egg, milk, peanut, soy, wheat, and. fish by CAP System FEIA. Sera were randomly selected from 300 stored samples of children and adolescents who had been evaluated by history, skin prick tests, and DBPCFCs. The study population was highly atopic; all patients had atopic dermatitis, and approximately 50% had asthma and allergic rhinitis at the time of initial evaluation. The performance characteristics of the CAP System FEIA were compared with those of skin prick tests and the outcome of DBPCFCs or "convincing" histories of anaphylactic reactions. Results: The prevalence of specific food allergies in the study population varied from 22% for wheat to 73% for egg. Allergy to egg, milk, peanut, and soy accounted for 87% of confirmed reactions. The performance characteristics of skin prick tests and CAP System FEIA (egg, milk, peanut, fish) were comparable, with excellent sensitivity and negative predictive accuracy but poor specificity and positive predictive accuracy. The performance characteristics of the CAP System FEIA for soy and wheat were poor. For egg, milk peanut, and fish allergy, diagnostic levels of IgE, which could predict clinical reactivity in this population with greater than 95% certainty, were identified: egg, 6 kilounits of **allergen** -specific IgE per liter (kU-A/L); milk, 32 kU-A/L; peanut, 15 kUA/L; and fish, 20 kU-A/L. Conclusions: When compared with the outcome of DBPCFCs, results of CAP System FEIA are generally comparable to those of skin prick tests in predicting symptomatic food hypersensitivity. Furthermore, by measuring the concentrations of food-specific IgE antibodies with the CAP System FEIA, it is possible to identify a subset of patients who are highly likely (gt 95%) to experience clinical reactions to egg, milk, peanut, or fish. This could eliminate the need to perform DBPCFCs in a significant number or patients suspected of having IgE-mediated food allergy.

L32 ANSWER 6 OF 11 MEDLINE

96384491 Document Number: 96384491. PubMed ID: 8792379. Characterization of ovomucoid-specific T-cell lines and clones from egg-allergic subjects. Eigenmann P A; Huang S K; **Sampson H A**. (Division of Pediatric Allergy and Immunology, Johns Hopkins University, School of Medicine, Baltimore, MD, USA.) PEDIATRIC ALLERGY AND IMMUNOLOGY, (1996 Feb) 7 (1) 12-21. Journal code: BU6; 9106718. ISSN: 0905-6157. Pub. country: Denmark. Language: English.

AB In the pathogenesis of allergic reactions, T cells and cytokines play a major role. However, characterizations of food **allergen**-specific T cells are very limited. In this study, we screened the peripheral blood mononuclear cells (PBMC) of 14 patients for reactivity to ovomucoid (Gal d I), the major hen's egg **allergen**, and ovalbumin (Gal d II). Cell lines and clones specific to ovomucoid were generated from PBMC of four egg-allergic subjects, in order to study antigen domain specificity and cell cytokine production profiles. The results demonstrated, firstly, that egg-allergic patients respond to ovomucoid rather than to ovalbumin, and, secondly, that antigen specificity is predominantly directed toward the

second and third domains of ovomucoid. The T-cell cytokine message was characterized by reverse transcriptase polymerase chain reaction (RT-PCR).

Cell lines and clones from all four patients consistently expressed interleukin (IL)-5. IL-4, IL-13, and interferon-gamma were found to be expressed only by certain lines or clones. This observation suggests a central pathogenic role for IL-5 in food allergy-related symptoms.

L32 ANSWER 7 OF 11 MEDLINE

94275035 Document Number: 94275035. PubMed ID: 8006309. Allergenicity and antigenicity of chicken egg ovomucoid (Gal d III) compared with ovalbumin (Gal d I) in children with egg allergy and in mice. Bernhisel-Broadbent J;

Dintzis H M; Dintzis R Z; **Sampson H A**. (Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1994 Jun) 93 (6) 1047-59. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB When attempting to generate mouse monoclonal antibodies to hen's egg ovalbumin, injection of commercially purified ovalbumin resulted in monoclonal antibodies, which when assayed against commercially purified ovalbumin (Gal d I) or ovomucoid (Gal d III), appeared to be specific to both. With the use of high-performance liquid chromatography (HPLC)-repurified ovalbumin and ovomucoid in assay procedures, monoclonal antibodies generated by commercially purified ovalbumin were found to be specific for ovomucoid only. To clarify this phenomenon, mice were serially injected with commercially purified ovalbumin or HPLC-repurified ovalbumin. It was found that most of the antibody response to commercially purified ovalbumin was directed against the minor (< 1%) ovomucoid contaminant and that HPLC-repurified ovalbumin failed to produce antibodies to ovomucoid. Commercially purified ovomucoid resulted in only minimal amounts of antibodies to ovalbumin. Thus when commercially purified ovalbumin is used both for immunization and immunoassay, most of the antibodies produced are actually against the small amount of ovomucoid contaminant, and not ovalbumin. To determine whether ovomucoid is the major antigenic and allergenic egg white protein in human beings, one group of 18 children with egg allergy were skin prick tested with half-log dilutions of egg white extract and diethylaminoethyl cellulose (DEAE)-repurified ovomucoid, ovalbumin, and lysozyme. Ovomucoid mean wheal diameters were significantly greater than wheal diameters in response to ovalbumin, lysozyme, and egg white extract at the three most concentrated of five dilutions tested: 0.01, 0.03, and 0.1 mg/ml ($p < 0.01$). Serum ovomucoid-specific IgE and IgG antibody concentrations to DEAE-repurified ovomucoid were significantly greater than that to DEAE-repurified ovalbumin ($p < 0.05$). In a second study, 10 patients with egg allergy and persistent egg hypersensitivity were compared with 11 patients with egg allergy in whom clinical tolerance to egg developed. IgE antibodies to repurified ovomucoid were significantly greater in patients with persistent egg hypersensitivity compared with patients in whom clinical tolerance developed at the time of both initial and follow-up food challenges. In contrast, there were no significant differences in IgE antibody concentrations to repurified ovalbumin in either group at any time. These results suggest that ovomucoid is the immunodominant protein

fraction in egg white and that the use of commercially purified ovalbumin has led to an overestimation of the dominance of ovalbumin as a major egg **allergen** and antigen in human beings.

L32 ANSWER 8 OF 11 MEDLINE
94007932 Document Number: 94007932. PubMed ID: 8404010. Food allergies in
children. Burks A W; **Sampson H.** (Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock.) CURRENT PROBLEMS IN PEDIATRICS, (1993 Jul) 23 (6) 230-52. Ref: 201. Journal code:
DVF; 1272515. ISSN: 0045-9380. Pub. country: United States. Language: English.

AB Ingested food represents the greatest foreign antigenic load that confronts the human immune system. In most individuals tolerance develops to food antigens that are continually gaining access to the body. When tolerance fails to develop, the immune system may react with a hypersensitivity reaction. Allergies to food affect up to 8% of children less than 3 years of age and 1% to 2% of the general population. Symptoms include the gastrointestinal, cutaneous, and respiratory symptoms, as well
as systemic anaphylaxis with shock. Clinical investigations in the past have characterized the food hypersensitivity disorders, but our understanding of the basic immunopathologic mechanism remains incomplete. Current progress in **allergen** characterization and the rigorous scientific methods now being applied to this field by many investigators provide hope that new information regarding the pathogenesis of these disorders and new forms of therapy will soon become available. For now, practicing physicians must carefully diagnose specific food sensitivities and educate patients and their families in the elimination of the responsible food **allergen**.

L32 ANSWER 9 OF 11 MEDLINE DUPLICATE 2
93099539 Document Number: 93099539. PubMed ID: 1464052. The antigenicity and allergenicity of microparticulated proteins: Simplesse. **Sampson H A**; Cooke S. (Department of Pediatrics, Johns Hopkins University, Baltimore, Maryland.) CLINICAL AND EXPERIMENTAL ALLERGY, (1992 Oct) 22 (10) 963-9. Journal code: CEB; 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.

AB New technologies are allowing the food industry to develop products from standard foods which may not be recognized in its modified form by food allergic patients. One such product, Simplesse, has been formulated by microparticulation of egg white and/or cows' milk proteins and is used as a fat substitute in many fat-laden foods. The purpose of this study was to
determine whether the process of microparticulation altered the allergenicity/antigenicity of egg white and cows' milk proteins compared to the starting materials. Soluble protein fractions of Simplesse and its respective starting materials were compared to egg white, cows' milk protein, an ultra-filtered egg white/condensed milk mixture, and/or a whey
concentrate by SDS-polyacrylamide gel electrophoresis. In addition, sera from 16 patients with documented egg and/or cows' milk hypersensitivity and two controls who were not allergic to egg or milk were used to assess potential allergenicity/antigenicity of these products by immunoblot (Western blot) analysis. There were heterogeneous IgE and IgG binding patterns to the food fractions among these food allergic patients suggesting differing sensitivity patterns among the individuals tested.

However, utilizing both SDS-PAGE and immunoblot analyses, the major **allergens** in the microparticulated products were the same as those found in the starting materials, egg and cows' milk. In addition, there was no evidence of 'novel' protein fractions in the Simplesse test materials compared to the starting materials.

L32 ANSWER 10 OF 11 MEDLINE DUPLICATE 3
92326874 Document Number: 92326874. PubMed ID: 1294076. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. **Sampson H A**; Mendelson L; Rosen J P. (Division of Pediatric Allergy and Immunology, Johns Hopkins University School of Medicine, Baltimore, MD.) NEW ENGLAND JOURNAL OF MEDICINE, (1992 Aug 6) 327 (6) 380-4. Journal code: NOW; 0255562. ISSN: 0028-4793. Pub. country: United States. Language: English.
AB BACKGROUND AND METHODS. Reports of fatal or near-fatal anaphylactic reactions to foods in children and adolescents are rare. We identified six children and adolescents who died of anaphylactic reactions to foods and seven others who nearly died and required intubation. All the cases but one occurred in one of three metropolitan areas over a period of 14 months. Our investigations included a review of emergency medical care reports, medical records, and depositions by witnesses to the events, as well as interviews with parents (and some patients). RESULTS. Of the 13 children and adolescents (age range, 2 to 17 years), 12 had asthma that was well controlled. All had known food allergies, but had unknowingly ingested the foods responsible for the reactions. The reactions were to peanuts (four patients), nuts (six patients), **eggs** (one patient), and milk (two patients), all of which were contained in foods such as candy, cookies, and pastry. The six patients who died had symptoms within 3 to 30 minutes of the ingestion of the **allergen**, but only two received epinephrine in the first hour. All the patients who survived had symptoms within 5 minutes of **allergen** ingestion, and all but one received epinephrine within 30 minutes. The course of anaphylaxis was rapidly progressive and uniphasic in seven patients; biphasic, with a relatively symptom-free interval in three; and protracted in three, requiring intubation for 3 to 21 days. CONCLUSIONS. Dangerous anaphylactic reactions to food occur in children and adolescents. The failure to recognize the severity of these reactions and to administer epinephrine promptly increases the risk of a fatal outcome.

L32 ANSWER 11 OF 11 MEDLINE
88116384 Document Number: 88116384. PubMed ID: 3123539. Double-blind placebo-controlled trial of oral cromolyn in children with atopic dermatitis and documented food hypersensitivity. Burks A W; **Sampson H A**. (University of Arkansas, Fayetteville.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1988 Feb) 81 (2) 417-23. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB Ten children with challenge-proven egg hypersensitivity and atopic dermatitis were enrolled in a double-blind crossover trial of oral cromolyn sodium. After receiving up to 40 mg/kg/day of cromolyn or placebo for 1 week, patients underwent double-blind placebo-controlled oral food challenges. In the eight subjects who reacted to the food challenge, there was no significant difference in the amount of food **allergen** eliciting the positive response, the timing of onset until first

subjective or objective symptoms developed, symptoms provoked, or the duration of the symptoms in either phase of the study. This study demonstrates no benefit in the treatment of children with atopic dermatitis and food hypersensitivity with oral cromolyn sodium.

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(FILE 'HOME' ENTERED AT 18:31:19 ON 05 JUN 2001)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 18:31:32 ON 05 JUN 2001

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L1         91377 S ALLERGEN
L2          2043 S L1 AND MODIFIED
L3           804 S L2 AND IGE
L4           114 S L3 AND IGE BINDING
L5             3 S L4 AND IGG BINDING
L6             3 DUP REMOVE L5 (0 DUPLICATES REMOVED)
L7             1 S L4 AND AMINO ACID SUBSTITUTION
L8           105 S L3 AND AMINO ACID
L9             7 S L3 AND AMINO ACID SUBSTITUTION
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FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 18:36:53 ON 05 JUN 2001

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L10        91377 S ALLERGEN
L11         2043 S L10 AND MODIFIED
L12            7 S L11 AND AMINO ACID SUBSTITUTION
L13            4 DUP REMOVE L12 (3 DUPLICATES REMOVED)
L14            0 S L11 AND AMINO ACID DELETION
L15            0 S L11 AND AMINO ACID ADDITION
L16          114 S L11 AND IGE BINDING
L17            4 S L16 AND DECREASE
L18            2 DUP REMOVE L17 (2 DUPLICATES REMOVED)
L19           49 DUP REMOVE L16 (65 DUPLICATES REMOVED)
L20         1793 S (BANNON G?/AU OR BURKS W?/AU OR SAMPSON H?/AU OR SOSIN
H?/AU)
L21          399 S L20 AND ALLERGEN
L22          221 S L21 AND PEANUT
L23          114 DUP REMOVE L22 (107 DUPLICATES REMOVED)
L24           71 S L23 AND IGE
L25            3 S L24 AND AMINO ACID SUBSTITUTION
L26            3 DUP REMOVE L25 (0 DUPLICATES REMOVED)
L27           15 S L21 AND LEGUMES
L28            9 DUP REMOVE L27 (6 DUPLICATES REMOVED)
L29            0 S L21 AND MILKS
L30            1 S L21 AND GRAINS
L31           16 S L21 AND EGGS
L32           11 DUP REMOVE L31 (5 DUPLICATES REMOVED)
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=> s l21 and fish

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L33           31 L21 AND FISH
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=> dup remove l33

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PROCESSING COMPLETED FOR L33
L34           17 DUP REMOVE L33 (14 DUPLICATES REMOVED)
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=> d l34 1-17 cbib abs

L34 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2001 ACS
2000:628260 Document No. 133:221613 Site-specific mutated **allergens** for decreased clinical reaction to allergy. **Bannon, Gary A.**; Burks, A. Wesley, Jr.; **Sampson, Hugh A.**; **Sosin, Howard B.**; King, Nina E.; Maleki, Soheila J.; Connaughton, Cathie; Kopper, Randall A.; Rabjohn, Patrick A.; Shin, David S.; Compadre, Cesar M. (The Board of Trustees of the University of Arkansas, USA; Mount Sinai School of Medicine of New York University). PCT Int. Appl. WO 2000052154 A2 20000908, 38 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US5487 20000302. PRIORITY: US 1999-PV122566 19990302; US 1999-PV122960 19990303;
US 1999-267719 19990311; US 2000-494096 20000128.
AB It has been detd. that **allergens**, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the IgE-binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compd. that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of IgE-binding sites. The crit. amino acids within each of the IgE-binding epitopes of the peanut protein that are important to Ig binding were detd. Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to IgE binding.

L34 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2001 ACS
2000:628031 Document No. 133:221612 Animal model of allergies. **Sampson, Hugh A.** (Mount Sinai School of Medicine of New York University, USA). PCT Int. Appl. WO 2000051647 A2 20000908, 124 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US5655 20000303. PRIORITY: US 1999-PV122960

19990303; US 1999-455294 19991206.

AB The authors disclose an animal model for studying allergic reactions. An animal is sensitized to a selected antigen by administering the antigen (e.g., milk) itself or a nucleic acid encoding the antigen (peanut **allergen**). Preferred antigens are anaphylactic antigens. The sensitized animal can then be used to screen for compds. which may help to prevent, ameliorate, or cure allergic conditions in humans.

L34 ANSWER 3 OF 17 MEDLINE DUPLICATE 1

2000387408 Document Number: 20314552. PubMed ID: 10856139. Quantitative IgE antibody assays in allergic diseases. Yunginger J W; Ahlstedt S; Eggleston P A; Homburger H A; Nelson H S; Ownby D R; Platts-Mills T A; **Sampson H A**; Sicherer S H; Weinstein A M; Williams P B; Wood R A; Zeiger R S. (Allergic Diseases Research Laboratory and the Department of Laboratory Medicine and Pathology, Mayo Clinic and Foundation, Rochester, MN 55905, USA.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (2000 Jun) 105 (6 Pt 1) 1077-84. Ref: 49. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB During the past several years, immunoassays for specific IgE antibodies have been refined to permit reporting results in mass units. Thus quantitative immunoassays for IgE antibodies may be an adjunct to skin tests. In cases of food allergy among children with atopic dermatitis, cutoff values for IgE antibody concentrations to egg, milk, peanut, and **fish** have been derived to provide 95% positive and 90% negative predictive values. Food-specific IgE antibody determinations can also be used to predict which food allergies are resolving spontaneously. Elevated egg-specific IgE antibody levels in infancy are associated with significantly increased risk for development of inhalant allergies later in childhood. In cases of inhalant allergy, specific IgE antibody levels correlate closely with results of inhalation challenge studies in cat-sensitive persons. Also, mite-specific IgE antibody levels correlate significantly with the mite **allergen** contents of reservoir dust in the homes of mite-sensitive persons. Immunoassays for quantitation of specific IgE antibodies may be used to document **allergen** sensitization over time and to evaluate the risk of reaction on **allergen** exposure. However, immunoassays and skin tests are not entirely interchangeable, and neither will replace the other in appropriate circumstances.

L34 ANSWER 4 OF 17 MEDLINE DUPLICATE 2

2001291384 Document Number: 21268341. PubMed ID: 11359629. Food anaphylaxis. **Sampson H A**. (Department of Pediatrics, Box 1198, Mount Sinai School of Medicine, One Gustave L Levy Place, New York, NY 10029-6574, USA.) BRITISH MEDICAL BULLETIN, (2000) 56 (4) 925-35. Ref: 39. Journal code: B4G; 0376542. ISSN: 0007-1420. Pub. country: England: United Kingdom. Language: English.

AB Food anaphylaxis is now the leading single cause of anaphylactic reactions treated in emergency departments in Westernized countries. In the US, it is estimated that there are 29,000 anaphylactic reactions to foods treated in emergency departments and 125-150 deaths each year. Peanuts, tree nuts, **fish** and shellfish account for the vast majority of severe food anaphylactic reactions. Immunopathogenic mechanisms responsible for food anaphylaxis may differ somewhat from other forms of anaphylaxis, since

elevation of serum tryptase is rarely seen following food anaphylactic reactions. Education regarding the strict avoidance of food **allergens**, the early recognition of anaphylactic symptoms, and the early use of self-injectable epinephrine remain the mainstays of therapy. However, clinical trials are now underway for the treatment of patients with peanut anaphylaxis utilizing anti-IgE antibody therapy and novel immunomodulatory therapies utilizing 'engineered' recombinant proteins, overlapping peptides, and immunostimulatory deoxyoligonucleotide sequences are being tested in animal models of anaphylaxis.

L34 ANSWER 5 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
2000:140358 Document No.: PREV200000140358. Pattern of food hypersensitivity over a decade of oral food challenges in children with atopic dermatitis. Ellman, L. K. (1); Chatchatee, P. (1); **Sampson, H. A. (1)**; Sicherer, S. H. (1). (1) Mount Sinai School of Medicine, New York, NY USA.
Journal of Allergy and Clinical Immunology., (Jan., 2000) Vol. 105, No. 1 part 2, pp. S182-S183. Meeting Info.: 56th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. San Diego, California, USA March 03-08, 2000 American Academy of Allergy, Asthma and Immunology. ISSN: 0091-6749. Language: English. Summary Language: English.

L34 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2001 ACS
1999:495482 Document No. 131:143531 Prognostic allergy or inflammation test.
Sampson, Hugh A. (USA). PCT Int. Appl. WO 9939211 A1 19990805, 30 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US1832 19990128. PRIORITY: US 1998-PV73171 19980130.
AB One can predict the likelihood a child will outgrow an allergy, esp. a food allergy, by screening for IgE antibodies immunoreactivities with linear vs. conformational epitopes. The child is first screened using std. techniques to det. what antigens the child is allergic to. The Igs in the sample from the patient are then characterized either using the natural purified antigen, recombinant antigen, reduced and alkylated antigen, proteolytic fragments of the antigen or synthetic peptides of between 4 and 40 amino acids in length, which can be immobilized for rapid and accurate screening. The antibodies from the patient are reacted with the protein or peptides to det. which peptides are bound by the antibodies. These antibodies are then characterized to det. if the epitopes they bind are linear or conformational. Those patients having antibodies primarily reactive with conformational epitopes will typically outgrow their allergies. A similar method for evaluation of IgG antibodies can be used to predict the prognosis of certain inflammatory disorders.

L34 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2001 ACS
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. **Sosin, Howard; Bannon, Gary A.**; Burks, A. Wesley, Jr.; **Sampson, Hugh A.** (University of Arkansas,

USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129.

PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.

AB It has been detd. that **allergens**, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compd. that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of IgE binding sites. The crit. amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to IgE binding.

L34 ANSWER 8 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 3

1999224853 EMBASE Food allergy. Part 1: Immunopathogenesis and clinical disorders. **Sampson H.A.**. Dr. H.A. Sampson, Department of Pediatrics, Box 1198, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY 10029-6574, United States. Journal of Allergy and Clinical Immunology 103/5 I (717-728) 1999.

Refs: 148.

ISSN: 0091-6749. CODEN: JACIBY. Pub. Country: United States. Language: English. Summary Language: English.

AB Up to 8% of children less than 3 years of age and approximately 2% of the adult population experience food-induced allergic disorders. A limited number of foods are responsible for the vast majority of food-induced allergic reactions: milk, egg, peanuts, **fish**, and tree nuts in children and peanuts, tree nuts, **fish**, and shellfish in adults. Food-induced allergic reactions are responsible for a variety of symptoms involving the skin, gastrointestinal tract, and respiratory tract and may be caused by IgE- mediated and non-IgE-mediated mechanisms. In part 1 of this series, immunopathogenic mechanisms and clinical disorders of food allergy are described.

L34 ANSWER 9 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

1999251951 EMBASE Anaphylaxis and food hypersensitivity. Burks A.W. Jr.; Jones S.M.; Wheeler J.G.; **Sampson H.A.**. Dr. A.W. Burks Jr., Department of Pediatrics, University Arkansas Medical Sciences, Arkansas

Children's Hospital, 1120 Marshall Street, Little Rock, AR 72202, United States. Immunology and Allergy Clinics of North America 19/3 (533-552) 1999.
Refs: 66.
ISSN: 0889-8561. CODEN: INCAEP. Pub. Country: United States. Language: English. Summary Language: English.

AB Anaphylaxis is a syndrome that has diverse causes and a diverse presentation of symptoms associated with type I IgE-mediated hypersensitivity. Anaphylaxis is recognized by cutaneous, respiratory, gastrointestinal, and cardiovascular signs and symptoms that occur alone or together. Recent studies have highlighted the prevalence of food-induced anaphylactic reactions, and have shown that certain foods are the most common cause of anaphylaxis outside of the hospital. Foods that most often precipitate an anaphylactic episode in children are milk, eggs, and peanuts; in adults, most episodes are caused by peanuts, tree nuts, **fish**, and shellfish. An accurate diagnosis should be made in food-induced anaphylaxis so that the offending food **allergen** can be eliminated from the diet. New developments in the treatment of allergic disease, including immunotherapy, are likely to have a significant impact in this area.

L34 ANSWER 10 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 4
1999416916 EMBASE Biochemistry of food **allergens**. Stanley J.S.; **Bannon G.A.**. G.A. Bannon, Department of Pediatrics, Univ. of Arkansas for Med. Sciences, Little Rock, AR 72205, United States. Clinical Reviews in Allergy and Immunology 17/3 (279-291) 1999.
Refs: 53.
ISSN: 1080-0549. CODEN: CRVADD. Pub. Country: United States. Language: English.

L34 ANSWER 11 OF 17 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:762662 The Genuine Article (R) Number: 242FP. Food hypersensitivity and atopic dermatitis: Pathophysiology, epidemiology, diagnosis, and management. Sicherer S H (Reprint); **Sampson H A**. MT SINAI SCH MED, JAFFE FOOD ALLERGY INST, DIV ALLERGY & IMMUNOL, DEPT PEDIAT, 1 GUSTAVE L LEVY PL, NEW YORK, NY 10029 (Reprint). JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (SEP 1999) Vol. 104, No. 3, Part 2, Supp. [S], pp. S114-S122. Publisher: MOSBY-YEAR BOOK INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318. ISSN: 0091-6749. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Laboratory and clinical investigations over the past two decades have demonstrated that food allergy plays a pathogenic role in a subset of patients, primarily infants and children, with atopic dermatitis (AD), Approximately 40% of infants and young children with moderate to severe AD have food allergy, but identifying this subset of patients and isolating the relevant food **allergens** requires a high index of suspicion, the use of appropriate laboratory tests, and, in some cases, physician-supervised oral food challenges, Removal of the causal food protein(s) leads to clinical improvement but requires a great deal of education because most of the common causal foods (egg, milk, wheat, soy, peanut, and so forth) are ubiquitous in the food supply, and food elimination diets risk causing nutritional deficits. Fortunately, most

food allergies resolve in early childhood, and food allergy is not a common cause for AD in older children and adults.

L34 ANSWER 12 OF 17 MEDLINE
1998374555 Document Number: 98374555. PubMed ID: 9481027. Prevalence of IgE-mediated food allergy among children with atopic dermatitis.
Eigenmann
P A; Sicherer S H; Borkowski T A; Cohen B A; **Sampson H A**.
(Department of Pediatrics, University of Geneva, Geneva, Switzerland.)
PEDIATRICS, (1998 Mar) 101 (3) E8. Journal code: OXV; 0376422. ISSN: 1098-4275. Pub. country: United States. Language: English.
AB OBJECTIVE: There is a growing body of clinical and laboratory evidence to support the notion that food allergy plays a role in the pathogenesis of atopic dermatitis (AD). However, the incidence of IgE-mediated food allergy in children with AD is not well established. DESIGN: A prospective study to determine the prevalence of IgE-mediated food hypersensitivity among patients referred to a university-based dermatologist for evaluation of AD. SETTING: University hospital pediatric dermatology clinic. PATIENTS: A total of 63 patients with AD were recruited (35 male; 32 white, 24 African-American, 7 Asian). METHODS: Patients were assigned an AD symptom score (SCORAD) and were screened for food-specific serum IgE antibodies to six foods (milk, egg, wheat, soy, peanut, **fish**) known to be the most allergenic in children. The levels of food-specific serum IgE were determined by the CAP System fluoroscein-enzyme immunoassay (CAP); patients with a value >/=0.7 kIUa/L were invited for an additional allergy evaluation. Those with CAP values below the cutoff were considered not food allergic. Patients were considered to be allergic if they met one of the following criteria for at least one food: 1) reaction on food challenge; 2) CAP value more than the 95% confidence interval predictive for a reaction; 3) convincing history of an acute significant (hives, respiratory symptoms) reaction after the isolated ingestion of a food to which there was a positive CAP or prick skin test. RESULTS: A total of 63 patients (median age, 2.8 years; median SCORAD, 41.1) were recruited; 22 had negative CAP values (without a significant difference in age or SCORAD score, compared with the 41 with positive specific IgE values). Further allergy evaluation was offered to the 41 remaining patients; 10 were lost to follow-up and 31 were evaluated further. Of these, 19 underwent a total of 50 food challenges (36 double-blind, placebo-controlled, and 14 open), with 11 patients experiencing 18 positive challenges (94% with skin reactions). Additionally, 6 patients had a convincing history with a predictive level of IgE; 5 had a convincing history with positive, indeterminate levels of IgE; and 1 had predictive levels of IgE (to egg and peanut) without a history of an acute reaction. Overall, 23/63 (37%; 95% confidence interval, 25% to 50%) had clinically significant IgE-mediated food hypersensitivity without a significant difference in age or symptom score between those with or without food allergy. CONCLUSIONS: Approximately one third of children with refractory, moderate-severe AD have IgE-mediated clinical reactivity to food proteins. The prevalence of food allergy in this population is significantly higher than that in the general population, and an evaluation for food allergy should be

considered in these patients.

L34 ANSWER 13 OF 17 MEDLINE DUPLICATE 5
97478240 Document Number: 97478240. PubMed ID: 9338535. Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. **Sampson H A**; Ho D G. (Johns Hopkins University School of Medicine, Baltimore, MD 21287-3923, USA.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1997 Oct) 100 (4) 444-51. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: The double-blind, placebo-controlled food challenge (DBPCFC) is the "gold standard" for diagnosis of food hypersensitivity. Skin prick tests and RASTs are sensitive indicators of food-specific IgE antibodies but poor predictors of clinical reactivity. Previous studies suggested that high concentrations of food-specific IgE antibody were predictive of food-induced clinical symptoms. Because the CAP System FEIA (Pharmacia Diagnostics, Uppsala, Sweden) provides a quantitative assessment of **allergen**-specific IgE antibody, this study was undertaken to determine the potential utility of the CAP System FEIA in diagnosis of IgE-mediated food hypersensitivity. METHODS: Sera from 196 patients with food allergy were analyzed for specific IgE antibodies to egg, milk, peanut, soy, wheat, and **fish** by CAP System FEIA. Sera were randomly selected from 300 stored samples of children and adolescents who had been evaluated by history, skin prick tests, and DBPCFCs. The study population was highly atopic; all patients had atopic dermatitis, and approximately 50% had asthma and allergic rhinitis at the time of initial evaluation. The performance characteristics of the CAP System FEIA were compared with those of skin prick tests and the outcome of DBPCFCs or "convincing" histories of anaphylactic reactions. RESULTS: The prevalence of specific food allergies in the study population varied from 22% for wheat to 73% for egg. Allergy to egg, milk, peanut, and soy accounted for 87% of confirmed reactions. The performance characteristics of skin prick tests and CAP System FEIA (egg, milk, peanut, **fish**) were comparable, with excellent sensitivity and negative predictive accuracy but poor specificity and positive predictive accuracy. The performance characteristics of the CAP System FEIA for soy and wheat were poor. For egg, milk, peanut, and **fish** allergy, diagnostic levels of IgE, which could predict clinical reactivity in this population with greater than 95% certainty, were identified: egg, 6 kilounits of **allergen** -specific IgE per liter (kU[A]/L); milk, 32 kU(A)/L; peanut, 15 kU(A)/L; and **fish**, 20 kU(A)/L. CONCLUSIONS: When compared with the outcome of DBPCFCs, results of CAP System FEIA are generally comparable to those of skin prick tests in predicting symptomatic food hypersensitivity. Furthermore, by measuring the concentrations of food-specific IgE antibodies with the CAP System FEIA, it is possible to identify a subset of patients who are highly likely (>95%) to experience clinical reactions to egg, milk, peanut, or **fish**. This could eliminate the need to perform DBPCFCs in a significant number of patients suspected of having IgE-mediated food allergy.

L34 ANSWER 14 OF 17 SCISEARCH COPYRIGHT 2001 ISI (R)
97:215851 The Genuine Article (R) Number: WM422. Clinical reactivity to beef in children allergic to cow's milk. Werfel S J; Cooke S K; **Sampson H A (Reprint)**. JOHNS HOPKINS UNIV HOSP, CMSC 1102, 600 N WOLFE ST, BALTIMORE, MD 21287 (Reprint); JOHNS HOPKINS UNIV, SCH MED, DEPT PEDIAT,

DIV ALLERGY IMMUNOL, BALTIMORE, MD 21205. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (MAR 1997) Vol. 99, No. 3, pp. 293-300. Publisher: MOSBY-YEAR BOOK INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318. ISSN: 0091-6749. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: Cow's milk is one of the most common food **allergens** in children. Limited Information is available on the prevalence of reactivity to a related food source, beef. The purposes of this study were to examine the prevalence of symptomatic sensitivity to beef in a selected pediatric population and to determine the frequency of concomitant reactivity to cow's milk and beef.

Methods: Children referred for assessment of atopic dermatitis and possible food hypersensitivity were evaluated for symptomatic reactivity to beef by double-blind placebo-controlled food challenges (DBPCFCs) and subsequent open feedings of beef. Sodium dodecyl-sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), immunoblot, and immunodot blot analyses were performed with patients' sera on preparations of beef extracts subjected to different cooking conditions: raw (no heating), medium, and well-cooked.

Results: Eleven of 335 children referred for evaluation of atopic dermatitis and possible food hypersensitivity were found to have symptomatic sensitivity to beef; eight were also sensitive to milk, as demonstrated in previous DBPCFCs. Eight patients reacted to beef during DBPCFC, and three tolerated beef in a DBPCFC and well-cooked beef in an open challenge but reacted to ingestion of less well-cooked beef. SDS-PAGE of raw beef revealed at least 24 protein fractions. Several protein bands in raw beef appeared to denature with heating. Bovine serum albumin and bovine gamma globulin were heat-labile in the beef extract, but six protein fractions persisted even after heating the beef extract for 2 hours at 85 degrees C. IgE from patients reacting to rare and well-cooked beef bound up to six of these heat-resistant fractions, but IgE from patients reacting only to rare beef failed to bind any of these fractions with one exception. in addition, patients reacting to rare and well-cooked beef had specific IgE to a 17.8 kd fraction, which was only weakly recognized by one patient reacting only to rare beef.

Conclusions: Specific IgE antibodies to heat-labile beef proteins might explain why some patients can tolerate well-cooked beef but not medium-rare and rare beef. Patients reacting only to rare beef may not need to maintain a complete beef elimination diet.

L34 ANSWER 15 OF 17 MEDLINE

94007932 Document Number: 94007932. PubMed ID: 8404010. Food allergies in children. Burks A W; **Sampson H**. (Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock.) CURRENT PROBLEMS IN PEDIATRICS, (1993 Jul) 23 (6) 230-52. Ref: 201. Journal code: DVF; 1272515. ISSN: 0045-9380. Pub. country: United States. Language: English.

AB Ingested food represents the greatest foreign antigenic load that confronts the human immune system. In most individuals tolerance develops to food antigens that are continually gaining access to the body. When tolerance fails to develop, the immune system may react with a

hypersensitivity reaction. Allergies to food affect up to 8% of children less than 3 years of age and 1% to 2% of the general population. Symptoms include the gastrointestinal, cutaneous, and respiratory symptoms, as well as systemic anaphylaxis with shock. Clinical investigations in the past have characterized the food hypersensitivity disorders, but our understanding of the basic immunopathologic mechanism remains incomplete. Current progress in **allergen** characterization and the rigorous scientific methods now being applied to this field by many investigators provide hope that new information regarding the pathogenesis of these disorders and new forms of therapy will soon become available. For now, practicing physicians must carefully diagnose specific food sensitivities and educate patients and their families in the elimination of the responsible food **allergen**.

L34 ANSWER 16 OF 17 MEDLINE DUPLICATE 6
93017542 Document Number: 93017542. PubMed ID: 1401644. **Fish** hypersensitivity. II: Clinical relevance of altered **fish** allergenicity caused by various preparation methods. Bernhisel-Broadbent J; Strause D; **Sampson H A**. (Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1992 Oct) 90 (4 Pt 1) 622-9. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB In double-blind, placebo-controlled, oral food challenges with **fish**, a 12-fold higher false-negative rate was found compared with other food antigens. In an effort to elucidate this discrepancy, cooked lyophilized **fish** extracts (used in double-blind, placebo-controlled, oral food challenges) were compared with cooked, nonlyophilized **fish** extracts (used in open challenges) by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, immunoblot, and ELISA-inhibition assays. Altered **fish** allergenicity as a result of food processing was examined with canned tuna and salmon. Forty-five children and young adults with food allergies, including 18 patients with IgE-mediated hypersensitivity to **fish**, were challenged with canned tuna. All 45 challenges with canned tuna were negative. Two of these patients are allergic to salmon and also have negative reactions to challenges with canned salmon. In vitro investigation by sodium dodecyl sulfate-polyacrylamide gel electrophoresis of tuna and salmon extracts revealed a striking loss of definable protein fractions in the canned **fish** extract when compared with raw and cooked **fish** extracts, and immunoblot analyses demonstrated minimal IgE-specific binding to the canned **fish** extracts. In addition, decreased allergenicity of the canned tuna and salmon was demonstrated by ELISA-inhibition assay and by negative oral challenges with canned salmon in two patients allergic to salmon. Collectively, these findings suggest that some of the major **allergens** responsible for IgE-mediated food allergy to **fish** are more labile than previously recognized.

L34 ANSWER 17 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
93021065 EMBASE Document No.: 1993021065. Genetic and environmental factors affecting the development of atopy through age 4 in children of atopic parents: A prospective randomized study of food **allergen** avoidance. Zeiger R.S.; Heller S.; Mellon M.H.; Halsey J.F.; Hamburger R.N.; **Sampson H.A.**. Department of Allergy-Immunology, Kaiser Permanente Medical Center, 7060 Clairemont Mesa Boulevard,San Diego, CA 92111, United States. Pediatric Allergy and Immunology 3/3 (110-127)

1992.
ISSN: 0905-6157. CODEN: PALUEE. Pub. Country: Denmark. Language: English. Summary Language: English.

AB The effect of food **allergen** avoidance, as well as other environmental and genetic factors, on the development of atopy were determined in this follow-up report of a prospective randomized controlled study of 288 infants of atopic parents, in which 78% were available for evaluation at age 4 years. The prophylactic-treated group consisted of mothers who avoided cow milk, egg, and peanut during the last trimester of pregnancy and lactation and of infants who avoided cow milk until 1 year (casein hydrolysate supplementation prior to 1 year) and egg, peanut, and **fish** until after 2 years. The control group consisted of maternal/infant pairs who followed standard feeding practices. The cumulative prevalence of food allergy and food sensitization remained lower in the prophylactic-treated group from 1 to 4 years of age. However, the period (current) prevalence of food allergy in both study groups was similar (about 5%) at 3 and 4 years. Such findings suggest that period prevalence may represent the more appropriate measure to assess the impact of intervention measures on the development of atopic disease at older ages. Prophylactic-treated children evidenced lower levels of IgG beta-lactoglobulin (BLG) at 4 months and 1 and 2 years ($p < 0.0001$) and lower IgG ovalbumen/ovomucoid (OVA) levels only at 2 years ($p < 0.001$). Both groups evidenced similar prevalences of asthma, allergic rhinitis, and positive inhalant skin tests from birth to 4 years. Children with food allergy evidenced higher 4 year cumulative prevalences of allergic rhinitis and asthma ($p < 0.05$). Risk factors for atopic disease by age 4 years were shown by multivariate analysis ($p < 0.05$) to include (1) unrestricted diet and elevated cord blood IgF with food allergy, (2) male gender and lower paternal level of education with asthma, and (3) non-caucasian ethnicity and spring/summer birth with atopic dermatitis and allergic rhinitis. Serum IgF levels were not significantly different between groups at 3 and 4 years, despite their being a trend towards lower serum IgE levels in the prophylactic-treated group at 4 months ($p < 0.07$). In the control group, formula feeding prior to 4 months was associated with higher 4 month serum IgE levels ($p < 0.05$). Stepwise linear regression revealed that serum IgE variability from birth to 4 years was influenced by male gender, non-caucasian ethnicity, maternal and paternal serum IgE levels, 4 month IgG BLG levels, positive food and inhalant skin tests, and the development of atopic dermatitis, food allergy, asthma, and allergic rhinitis. These findings demonstrate the strength of genetic factors and their modulation by dietary and environmental influences in the development of atopy and reveal that the reduction in food allergy in infancy by maternal/infant food **allergen** avoidance fails to affect respiratory allergy development from birth to 4 years.

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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